

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

John Alexander Edgar

Title:

ANTI CANCER AGENT AND

METHOD OF TREATMENT OF

**CANCER** 

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#### **CLAIM FOR CONVENTION PRIORITY**

Commissioner for Patents Washington, D.C. 20231

Sir:

The benefit of the filing date of the following prior foreign application filed in the following foreign country is hereby requested, and the right of priority provided in 35 U.S.C. § 119 is hereby claimed.

In support of this claim, filed herewith is a certified copy of said original foreign application:

AUSTRALIAN Patent Application No. PQ 3148 filed 09/29/1999.

Respectfully submitted,

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Date July 22, 2002

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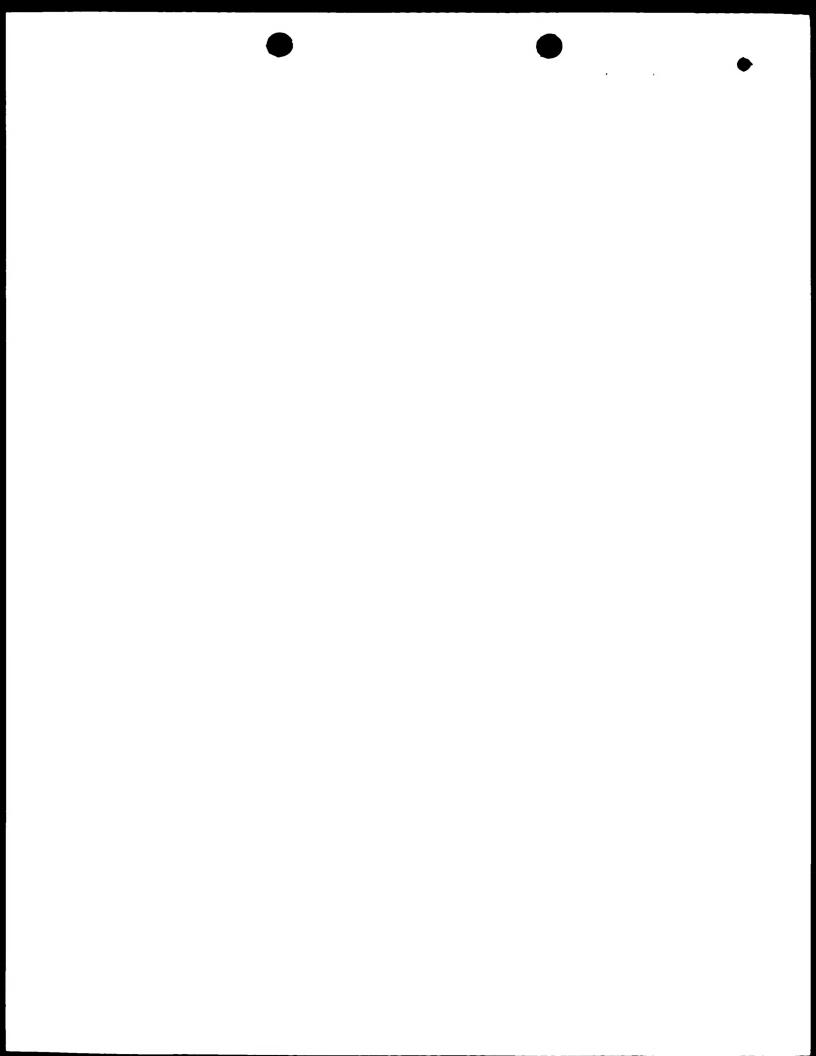
I. LEANNE MYNOTT. MANAGER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. PQ 3148 for a patent by COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION filed on 29 September 1999.

WITNESS my hand this Twenty-second day of May 2002

LEANNE MYNGTT

MANAGER EXAMINATION SUPPORT

AND SALES



### AUSTRALIA Patents Act 1990

### PROVISIONAL SPECIFICATION

Invention Title:ANTI CANCER AGENT AND METHOD OF TREATMENT OF CANCER

Applicant: COMMONWEALTH SCIENTIFIC & INDUSTRIAL RESEARCH ORGANISATION

The invention is described in the following statement:

#### ANTI CANCER AGENT AND METHOD OF TREATMENT OF CANCER

The present invention relates to the treatment of cancer and to compositions for use in treatment of cancer.

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The search for anti-cancer agents has been, and remains, a major endeavour of the pharmaceutical industry, academic institutions and government agencies throughout the world. One of the significant problems with many cancer treatments is the severe adverse affects they have on the patient and non-cancerous tissues.

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We have now found that phomopsin mycotoxins (hereafter referred to as phomopins) and their derivatives exhibit potent anticancer activity. We have also found that phomopsins exhibit selective activity against liver cancer. Without wishing to be bound by theory we believe that phomopsins exhibit selectivity for liver cancers due to a tendency of phomopsin to accumulate in the liver. It will be appreciated that the selectivity of phomopsin in treatment of liver cancer is a significant advantage as it allows liver cancers to be targeted while minimising the effects on other tissues.

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Phomopsin may however be utilised in treatment of cancers other than liver cancer by selecting formulations or derivatives of phomopsin which enhance selectivity of the drug for certain types of cancer cells or certain types of cancers. Derivatives of phomopsins may be formed which are conjugates with monoclonal antibodies. The monoclonal antibody may be produced by known methods to provide selectivity for cancer cells.

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Phomopsins are characterised by a 13-member ring structure generally of formula I

Y OH

$$X \longrightarrow O$$
 $R^1$ 
 $C \longrightarrow R^2$ 
 $C \longrightarrow R^3$ 
 $C \longrightarrow R^4$ 
 $C \longrightarrow C$ 
 $C$ 

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#### wherein

R1, R2, R3, R4, R5, R6 and R7 are optional substituents and may be independently selected from the group consisting of hydrogen, aliphatic, aromatic, peptide chains and halogen.

- X is aliphatic, hydrogen or halogen (preferably hydrogen); and Y is aliphatic, hydrogen or halogen (preferably chlorine); where present a peptide chain may be conjugated with a monoclonal antibody (Mab).
- The preferred phomopsins and phomopsin derivatives are those containing the group of formula Ia:

CI OH

OH

OR

$$R^{1}$$
 $C - R^{2}$ 
 $C - R^{2}$ 
 $C - R^{3}$ 
 $C - R^{3}$ 
 $C - R^{4}$ 
 $C - R$ 

- In formula I and Ia R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> may typically be independently selected from hydrogen and aliphatic and R<sup>4</sup> is generally a peptide. In one embodiment R<sup>4</sup> is a peptide conjugated with an antibody, particularly a monoclonal antibody (Mab). More preferably R<sup>1</sup>, R<sup>2</sup>, R<sup>5</sup> and R<sup>6</sup> are lower aliphatic and R<sup>3</sup> and R<sup>7</sup> are hydrogen. Even more preferably R<sup>1</sup>, R<sup>2</sup> and R<sup>6</sup> are lower alkyl and R<sup>6</sup> is lower alkyl or lower alkenyl. Most preferably R<sup>1</sup> is ethyl, R<sup>2</sup> is methyl, R<sup>3</sup> is hydrogen, R<sup>5</sup> is isopropyl or iso-propenyl and R<sup>6</sup> is methyl. Where used herein the terms lower aliphatic, lower alkyl and, lower alkenyl include groups containing up to six carbon atoms and most preferably up to 4 carbon atoms.
- 30 The preferred stereochemistry of the compounds of formula Ia is as shown in formula Ib:

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CI OH

OH

OH

$$R^{1}$$
 $R^{2}$ 
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{5}$ 
 $R^{7}$ 
 $R^{7$ 

The group  $R^4$  is a peptide preferably a di- or tri-peptide which may be optionally bound to an antibody such as a monoclonal antibody. The preferred group  $R^4$  has the formula II:

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wherein the dotted line represents an optional double bond;

 ${\sf R}^8$  and  ${\sf R}^9$  are independently selected from hydrogen and lower alkyl and more preferably  ${\sf R}^8$  is methyl and  ${\sf R}^9$  is ethyl;

R12 is selected from the group consisting of amino, mono substituted amino, disubstituted amino and an amino acid residue particularly the group of formula III:

wherein  $R^{13}$  and  $R^{14}$  are hydrogen or together form a double bond and  $R^{15}$  is selected from the group consisting of hydroxy, amino, substituted amino or an antibody particularly Mab.

When R<sup>15</sup> is an antibody or linked to an antibody it is preferred that R<sup>13</sup> and R<sup>14</sup> form a double bond providing a dehydroaspartic acid residue. A dehydroaspartic acid residue has been found to facilitate delivery of phomopsin via a Mab conjugate.

The carbon-nitrogen bond in the residue of formula III is relatively weak enabling an active phomopsin of formula Ia (wherein in the group of formula II R<sup>12</sup> is amino) to be released from the MAb once it becomes bound to cancer cells.

The most preferred phomopsin compounds are selected from phomopsin A, octahydrophomopsin A, iso-phomopsin and phomopsinamine A. These compounds have the formula set out below:

In one aspect the invention provides a pharmaceutical composition for treatment of cancer, preferably liver cancer, containing a phomopsin compound or derivative thereof or pharmaceutically acceptable salt of the phomopsin or derivative and a pharmaceutically acceptable carrier.

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Salts of phomopsin such as the alkaline metal salts are reasonably water soluble. Aqueous solutions can be formed by dissolving the phomopsin in a dilute base such as sodium hydroxide to provide a neutral solution.

In another aspect the invention provides a method of treatment of a patient suffering cancer including administering to the patient a phomopsin compound or derivative thereof or pharmaceutically acceptable salt of the phomopsin or derivative.

The phomopsin compound may be administered by a variety of methods including oral administration in the form of a syrup, capsule, tablet or the like, by injection or by intravenous infusion.

Preferably the compound is administered by intravenous infusion

20 In a further aspect the invention provides the use of a phomopsin compound as hereinbefore described for preparation of a pharmaceutical composition for treatment of cancer and in particular liver cancer.

Phomopsin compounds are produced by certain fungi, including <u>Diaporte toxicus</u> (formerly <u>Phomopsis leptostromiformis</u>) and <u>Phomopsis emicis</u>, or may be derived from these natural products.

The isolation of phomopsin A is described by C. Culvenor, J. Edgar and M. Mackay, <u>Tetrahedron</u> Vol. 45, No. 8 pp 2351 (1989). Preparation of derivatives of phomopsins such as octahydrophomopsins are described by J. Edgar, J. Frahn, P. Cockrum and J. Culvenor in the paper "Lupinosis. The Chemistry and Biochemistry of the Phomopsins" <u>Mycotoxins and Phycotoxins</u>, collection of invited papers presented at the sixth International IUPAC Symposium on Mycotoxins and Phycotoxins, Pretoria, Rep. South Africa, 22-25 July 1985.

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The activity of phomopsin is believed to be due in part to the strong binding of the compound to tubulin. This may disrupt cell mitosis by inhibiting tubulin formation and cause depolymerization of formed microtubules. It may be preferred in some cases to use phomopsin in combination therapy with one or more other anticancer drugs or therapies. The drugs used in combination with phomopsin may be selected to enhance results by providing complementary activity in binding to microbubules. Examples of possible drugs for use in combination with phomopsin include paclitaxel, vinblastine, vincristine and alkaloids.

The present invention will now be more fully described with reference to the following examples. It should be understood, however, that the description following is illustrative only and should not be taken in any way as a restriction on the generality of the invention described above.

#### 15 Example 1

The following data demonstrate, the anticancer activity of phomopsin A, octahydrophomopsin A, iso-phomopsin A and phomopsinamine A against 60 human cancer cell lines *in vitro*. Phomopsin A and octahydrophomopsin A were obtained by the method as described in the references referred to above.

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Iso-phomopsin A and phomopsinamine were prepared as follows:

#### ISOLATION OF PHOMOPSIN A

#### Background:

The extraction process is designed to minimise difficulty and cost. The fermented seed is continuously extracted with recycling 15% methanol:water through an in line XAD (styrene divinylbenzene copolymer) column. The time required for adsorption of phomopsin A onto the XAD is quite lengthy, but requires minimal operator input. The timing of this step is not critical, hence can be adapted to suite operating conditions.

The phomopsin A has a relatively low solubility in 15% methanol. The procedure relies on the adsorption of phomopsin A on the XAD resin driving the solubility equilibrium of phomopsin A in the fermented seed toward dissolution. This

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procedure reduces solvent usage, volumes to be handled and flammability hazards. The alternate method of extraction, without recycling would use 150+ litres of pure methanol for the initial extraction, involve a further concentration step (or dilution of the methanol extract to 900+L) then adsorption onto XAD. The current procedure uses 12 L methanol, requires minimal operation input for the adsorption phase and uses far less solvent (total volume 85L instead of 900+L).

The elution of the concentrated phomopsin A from the column is the first step in a 3 stage isolation to produce crystalline phomopsin A of 80-90% purity.

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Phomopsin may be eluted from the collection using 15% methanol as a preliminary wash and 100% methanol to complete elution. Silica gel flash column chromatography may be used for purification. The column is conditioned using 5:95 amonia:isopropanol and the concentrate dissolved in a minimum of 20:65:15 ammonia:isopropanol:water. Phomopsin is eluted using this 3 solvent combination. Recrystallisation from boiling glacial acetic acid provides phomopsin in 80-90% purity.

#### PREPARATION OF iso-PHOMOPSIN A

#### 20 Materials:

0.05M HgCl<sub>2</sub>:

280 mg HgCl<sub>2</sub> dissolved in 2 ml H<sub>2</sub>O (+50  $\mu$ l 10M HCl).

Phomopsin A:

18.3 mg PhA dissolved in 2 ml H<sub>2</sub>O (with puff of NH<sub>3</sub>).

1M HCI

#### Method:

Phomopsin A (2.0 ml) was mixed with 0.05M HgCl<sub>2</sub> (1 ml) and 1M HCl (200 μl), total volume 3.2 ml, and left at room temperature for 5 hours. The solution was diluted to 8 ml then passed through a prepared C18 Maxi-clean SPE cartridge (900 mg) and washed with 7-8 ml H<sub>2</sub>O. The Maxi-clean was then eluted with 8-9 ml MeOH and made to 10 ml. The aqueous eluate from the first C18 cartridge was reprocessed through a second C18 cartridge to check whether the first cartridge was overloaded. The MeOH eluate from the second cartridge had very little residue on drying and was not included in further processing.

The methanol eluate was evaporated to dryness and subject to HPLC analysis and preparative HPLC.

Needle contamination with mercuric chloride was enough to cause almost complete conversion to iso-phomopsin. A needle used for a solution containing mercuric chloride could not be used for phomopsin, even with exhaustive washing. The phomopsin - HgCl<sub>2</sub> reaction mixture could be pumped back and forth through a disposable needle (20-30 times), a sample removed for assay, and the remainder of the sample left at RT for 5 hours, with hourly sampling (if necessary).

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#### PREPARATION OF PHOMOPSINAMINE

Phomopsin A (15.3 mg) was dissolved in 1M HCl and left at RT for 28 hours. The reaction mixture was diluted to 8 ml then passed through a strong anion exchange cartridge (SAX, 600 mg) to remove any unreacted phomopsin A (pH of solution expected to be @ 1.52). The aqueous eluate (+ washings) was then passed through a prepared C18 cartridge (900 mg), washed with  $H_2O$  (10 ml) then eluted with methanol (10 ml).

The methanol eluate was evaporated to dryness subject to HPLC analysis and preparative HPLC.

This method may be modified by sampling the reaction mixture after 5-6 hours, 24 hours and 28-30 hours. All washings and eluates may be assayed by HPLC to monitor the conversion of phomopsin to phomopsinamine.

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The methods used are those employed by the United States National Cancer Institute (NCI) as a primary screen for discovering compounds with anticancer potential (Boyd and Paull, 1995). The data are presented in the standard format used by NCI to show, for each compound tested, the absolute and relative sensitivity of individual cancer cell lines to the compounds and to demonstrate reproducible and selective effects.

#### HOLLOW FIBER ASSAY FOR PRELIMINARY IN VIVO TESTING

The Biological Testing Branch of the Developmental Therapeutics Program has adopted a preliminary in vivo screening tool for assessing the potential anticancer activity of compounds identified by the large scale in vivo cell screen. For these assays, human tumour cells are cultivated in polyvinylidene fluoride (PVDF) hollow fibers, and a sample of each cell line is implanted into each of two physiologic compartments (intraperitoneal and subcutaneous) in mice. Each test mouse receives a total of 6 fibers (3 intraperitoneally and 3 subcutaneously) representing 3 distinct cancer cell lines. Three mice are treated with potential antitumor compounds at each of 2 test doses by the intraperitoneal route using a QD x 4 treatment schedule. Vehicle controls consist of 6 mice receiving the compound diluent only. The fiber cultures are collected on the day following the last day of treatment. To assess anticancer effects, viable cell mass is determined for each of the cell lines using a formazan dye (MTT) conversion assay. From this, the %T/C can be calculated using the average optical density of the compound treated samples divided by the average optical density of the vehicle controls. In addition, the net increase in cell mass can be determined for each sample as a sample of fiber cultures are assessed for viable cell mass on the day of implantation into mice. Thus, the cytostatic and cytocidal capacities of the test compound can be assessed.

Generally, each compound is tested against a minimum of 12 human cancer cell lines. This represents a total of 4 experiments since each experiment contains 3 cell lines. The data are reported as %T/C for each of the 2 compound doses against each of the cell lines with separate values calculated for the intraperitoneal and subcutaneous samples.

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Compounds are selected for further *in vivo* testing in standard subcutaneous xenograft models on the basis of several hollow fiber assay criteria. These include: (1) a % T/C of 50 or less in 10 of the 48 possible test combinations (12 cell lines X 2 sites X 2 compound doses); (2) activity at a distance (intraperitoneal drug/subcutaneous culture) in a minimum of 4 of the 24 possible combinations; and/or (3) a net cell kill of 1 or more cell lines in either implant site. To simplify evaluation, a points system has been adopted which allows rapid viewing of the activity of a given compound. For this, a value of 2 is assigned for each compound dose which results in a 50% or greater reduction in viable cell mass. The

intraperitoneal and subcutaneous samples are scored separately so that criteria (1) and (2) can be evaluated. Compounds with a combined IP+SC score ≥ 20, a SC score  $\geq 8$  or a net cell kill of one or more cell lines are referred for xenograft testing. These criteria were statistically validated by comparing the activity outcomes of > 80 randomly selected compounds in the hollow fiber assay and in the xenograft testing. This comparison indicated that there was a very low probability of missing an active compound if the hollow fiber assay were used as the initial in vivo screening tool. In addition to these criteria, other factors (e.g. unique structure, mechanism of action) may result in referral of a compound for standard xenograft testing without the compound meeting these criteria.

#### SCREENING DATA REPORT COMPONENTS

#### The Calculated Measurement of Effect: Percentage Growth (PG)

The measured effect of the compound on a cell line is currently calculated according to one or the other of the following two expressions:

If (Mean  $OD_{test}$  - Mean  $OD_{tzero}$ )  $\geq 0$ , then

PG = 100 x (Mean OD<sub>test</sub> - Mean OD<sub>tzero</sub>)/(Mean OD<sub>ctrl</sub> - Mean OD<sub>tzero</sub>) If (Mean OD<sub>test</sub> - Mean OD<sub>tzero</sub>) < 0, then

PG = 100 x (Mean OD<sub>test</sub> - Mean OD<sub>tzero</sub>)/Mean OD<sub>tzero</sub>

20 Where:

> Mean ODtzero = The average of optical density measurements of SRB-derived color just before exposure of cells to the test compound.

> Mean ODtest = The average of optical density measurements of SRB-derived color after 48 hours exposure of cells to the test compound.

25 Mean OD<sub>ctrl</sub> = The average of optical density measurements of SRB-derived color after 48 hours with no exposure of cells to the test compound.

#### The Data Sheet:

This page of the data package represents the experimental data collected against each cell line. The first two columns describe the subpanel (e.g. leukemia) and cell line (e.g. CCRF-CEM) involved. The next two columns list the Mean ODtzero and Mean ODctrl; the next five columns list the Mean ODtest for each of five different concentrations. Each concentration is expressed as the log10 (molar or

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μg/ml). The next five columns list the calculated PGs for each concentration. The response parameters GI50, TGI, and LC50 are interpolated values representing the concentrations at which the PG is +50, 0, and -50, respectively. Sometimes these response parameters cannot be obtained by interpolation. If, for instance, all of the PGs in a given row exceed +50, then none of the three parameters can be obtained by interpolation. In such a case, the value given for each response parameter is the highest concentration tested and is preceded by a ">" sign. This practice is extended similarly to the other possible situations where a response parameter cannot be obtained by interpolation.

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#### **Dose-Response Curves:**

The dose-response curve page of the data package is created by plotting the PGs against the log<sub>10</sub> of the corresponding concentration for every cell line. The cell line curves are grouped by subpanel. Horizontal lines are provided at the PG values of +50, 0, and -50. The concentrations corresponding to points where the curves cross these lines are the G150, TG1, and LC50, respectively.

#### The Mean Graphs:

Mean graphs facilitate visual scanning of data for potential patterns of selectivity for particular cell lines or for particular subpanels with respect to a selected response parameter. Differences in apparent selectivity patterns may occur for the same compound against the same cell lines when different parameters are compared. The mean graphs page of the data package shows mean graphs at each of the principal response parameters: G150, TG1, and LC50. Bars extending to the right represent sensitivity of the cell line to the test agent in excess of the average sensitivity of all tested cell lines. Since the bar scale is logarithmic, a bar 2 units to the right implies the compound achieved the response parameter (e.g. G150) for the cell line at a concentration one-hundredth the mean concentration required over all cell lines, and thus the cell line is unusually sensitive to that compound. Bars extending to the left correspondingly imply sensitivity less than the mean. If, for a particular drug and cell line, it was not possible to determine the desired response parameter by interpolation, the bar length shown in either the highest concentration tested (and the listed log10 of the

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response parameter will be preceded by a ">") or the lowest concentration tested (and the listed  $log_{10}$  will be preceded by a "<").

The values at either limited (> or <) are also calculated in the mean used for the mean graph. Therefore, the mean used in the mean graph may not be the actual mean of the G150, for instance. For this reason, we shall refer to this value as the MG-MID (for mean graph midpoint).

#### National Cancer I

### titute Developmental Therapedics Program In-Vitro Testing Results

Experiment ID: 9502RM16 Test Type: 8 Units: Molar Port Date: March 28, 1995 Test Date: February 13, 1995 QNS: SHP MC:

OMI: Phomopsin A Stain Reagent: Dual-Pass SSPL: 0FLC

	T 2 ma		Ke i	an Critic	al Dens	Logi	Concer	tietion							
Panel/Cell Line	Zerc	Ctil	- £ . C	-7.0	-6.0	-5.0	-4.0	- 6 0	-7 0	cent ( -€.C	-: 0 F.C )		6710		
Leukemia							4.0	- 6 . 0	-7.0	- e . c	- 5.0	-4.0	G150	TGI	ಚರಕರ
CCRF-CEM	0.634	1.661	1.649		1.640		0.474	96	10 é	ع ب	34	- 24	5 55E-06	3.79E-C5	
HL-60 (TB)				1.645	1.363		0.337	101	101	76	-17	- 4 3	1.901-06	6 625-06	
K-562 HOLT-4		1.209	1.161	1.227	1.101	0.560	0.294	97	102	€ 🗅	24	-23	3.66106	3 245-05	12 000
RPMI-8226		1.747	1.733	1.761	1.698	1.143	0.995	öö	103	95	4.3	2 %	7.33E-06	>1.00E-04	>1.005-04
SR	0.755	0. R56	1.531	1.516	1.472	0.992		111	109		36	- 5	6.16E-06	7.61E-05	27 005 04
Non-Small Cell Lun	CADCE	· r	V. 323	0.096	0.666	0.406	0.315	116	111	5 4	-16	-35	1.15E-06	5.66E-06	1.00E-04
AS49/ATCC		1.362	1.363	1.389	1.055	0.681	0.54€	102	163						
EKVX	0.402	0.935	0.946	0.966	0.854		0.346	102	100	69 85	31 40	1 7	3.14E-06	>1.00E-04	·1.00E-04
HOP-62	0.391	0.953	0.974	0.985		0.796		104	100	9 (	72	1.	6.09E-06	11.00E-04	1.00E-04
HOP-92		1.260	1.329		1.309	1.217	1.211	114	116	110	و َ	9-)	>1.00E-04	1.00E-04	1.00E-04
NCI-H226		0.890	0.910	0.948	0.854	0.562	0.435	107	12:	67	- 2	-26	7 555-06	-1.00E-04	·1.00E-04
NCI-H23	0.419	1.205	1.246		1.214	1.003	0.717	105	102	101	74	3 6	4 658-05	9.03E-06 >1.00E-04	1.00E-04
NCI-H322H	0.624	1.629	1.653	1.612	1.567	0.931	0.702	102	9.5	94	3.0	٤	4.92E-06	>1.00E-04	71.00E-04
NCI-H460 NCI-H522	0.181	1.131	1.155	1.235	0.972	0.349	0.271	103		ε3	16	ب	3.21E-06	>1.00E-04	71.00E-04
Colon Cancer	0.413	0.954	0.966	0.963	0.952	0.513	0.32ε	103	105	100	16	-21	4.06E-06	2.97E-05	21.00E-04
COLO 205	0 326	1.242	1.303												
HCC-2996		1.321	1.303	1.263	0.849	0.151	0.068	107	75	57	-54	-70	1.15E-06	3.26E-06	9.21E-06
HCT-116			1.209	1.263	1.245	0.621	0.319	95 97	95	74	4	-46	2.23E-06	1.21E-05	>1.00E-04
HCT-15	0.317	1.751	1.611	1.714	1.383		0.466	90	102	. 101	32	11	5.47E-06	>1.00E-04	>1.00E-04
HT29		0.659	0.622		0.796			95	97	91	26 14	10 5	3.23E-06	>1.00E-04	>1.00E-04
ICH:1.2	0.294	1.232	1.230	1.07€	0.675	0.411		100	6.3	62	11:	5	3.42E-06	>1.00E-04	>1.00E-04
SW-620	0.156	1.016	0.962	1.077		0.692		96	107	101	62	44	1.745-06	>1.00E-04 >1.00E-04	>1.00E-04
CNS Cancer											01	• • • • • • • • • • • • • • • • • • • •	4.30E-03	>1.00E-04	>1.00E-04
SF-266	0.463		1.314		1.210	0.692		101	101	69	51	36	1.19E-05	>1.00E-04	>1 005-04
SF-295 SF-539	0.400		1.122		0.900			107	102	74	21	6	2.61E-06	>1.00E-04	>1.00E-04
SNB-19			0.854			0.317		94	94	60	-16	-54	1.64E-06	6.17E-06	7.795-05
SNB-75	0.361	1.452	0.610		1.363		0.762	93	97	92	44	22	7.56E-06	>1.00E-04	>1.00E-04
U251	0.169	0.626		0.571	0.500	0.339	0.432	93	77	4.6	-11	21	€.48E-07		>1.00E-04
Melanoma		0.031	0.633	0.863	0.776	0.302	0.225	100	101	€ 9	16	4	3.40E-06	>1.00E-04	>1.00E-04
LOX IMVI	0.191	1.076	0.966	1.053	0 922	0.574	0 377	90	97	62					
HRIME-3H	0.464	0.952	0.956	0.914	0.760		0.566	101	97	65	43 32	26	6.71E-06	>1.00E-04	>1.00E-04
124		0.527	0.521	0.472		0.198		98	£3	64		-27		>1.00E-04	
SK-MEL-2	0.746	1.404		1.375	1.297	0.954	0.616	97	95	84	32	11		1.04E-05 >1.00E-04	
SK-MEL-26	0.576		1.229	1.152	1.047	0.679	0.636	94	6.3	66	44	37		>1.00E-04	
SK-MEL-5 UACC-257	0.034	1.051	1.053	0.918		0.344		100	€7	4 8	30	23	6.89E-07	>1.00E-04	>1.00E-04
WACC-62		1.128		1.149		0.589		113	104	72	60	70		>1.00E-04	
Ovarian Cancer	0.3/1	1.790	1.796	1.735	1.533	1.043	0.667	101	ō.	70	3 €	2 €		>1.00E-04	
IGR-OV1	0.515	1.761	1 766	3 763	1 776										
OVCAR-3	0.293	0.611	1.748		0.623	1.429		90	101	97	73	44		>1.00E-04	
OVCAR-4	0.467	1.061			1.167			102	97 64	64	11	. 4		>1.00E-04	
OVCAR-5	0.393	0.867		0.572		0.465		101	103	114 78	63	54		>1.00E-04	
OVCAR-6	0.267	0.947	0.914			0.692		95	20.	97	20 61			>1.00E-04	
SK-OV-3	0.466	0.975	0.905	0.962		0.565		104	é n	70	10	11		>1.00E-04 >1.00E-04	
Renal Cancer									-				2.432-00	71.00E-04	>1.00E-04
766-0	0.200			0.640	0.828	0.389	0.325	105	9(	8.8	7.€	3.6	4 145-06	>1.00E-04	>3 00E=04
A498 ACHN	1.061	1.567	1.550		1.406			9.6	9:	67	-6	Č		9.31E-05	
CAKI-1	0.406	1.396	1.412	1.309	1.267	0.881	0.759	101	91	€ 5	46	36	6.65E-06	>1.00E-04	>1.00E-04
IV.F-393	0.466	1.545	0.691	0.864	0.762	0.641	0.597	90	88	63	37	2.€		>1.00E-04	
\$211.2C	0.371	1.34:			1.113	0.913		91	67	40	25	3 %		>1.00E-04	
TK-10	0.627	1 221		1.309			0.711	104	104	92	64	3 &		>1.00E-04	
00-31	0.593	1.442		1.367		1.032		94	101	8.5	33	5.3		>1.00E-04	
rostate Cancer			2.924	1.36,	1.369	1.134	0.997	96	94	91	64	4 €	7.06E-05	>1.00E-04	>1.00E-04
PC-3	0.302	1.096	1.092	1.010	0.625	0.465	0.360	100	ē c	66	20		2 22- 4-		
DU-145	0.339	1.061	1.122		0.617			106	102	66	20	10 -13		>1.00E-04	
sreast Cancer						2.220	- •	100	101	00	•	-13	1.691-06	2.42E-05	>1.00E-04
HCF7		1.174	1.156	1.115	0.924	0.563	0.465	96	92	€7	21	6	2 335-05	>1.00E-04	11 DOE-04
HCF7/ADR-RES	0.330		0.896	0.904	0.647	0.609		99	0.0	90	4 6	13		>1.00E-04	
MDA-ME-231/ATCC			0.954	0.965		0.634		و و	101	93	77	1		>1.00E-04	
HS 576T HDA-MB-435	0.564	1.319	1.337			1.165		104	107	101	71	75		>1.00E-04	
MDA-MB-435		0.961	0.968	0.647	0.427	0.174		96	60	16	-46	-60		1.63E-06	
BT - 54 9	0.214	0.752 0.821			0.152			6.3	71	-20	-66	-75	1.625-07	5.11E-07	2.32E-06
T-47D		2.002	0.622	0.693		0.664				112	60	56	>1.00E-04	>1.00E-04	>1.00E-04
	J. /11	2.002	1.666	2.094	7.626	1.252	1.655	51	107	71	42	73		>1.00E-04	1.00E-04

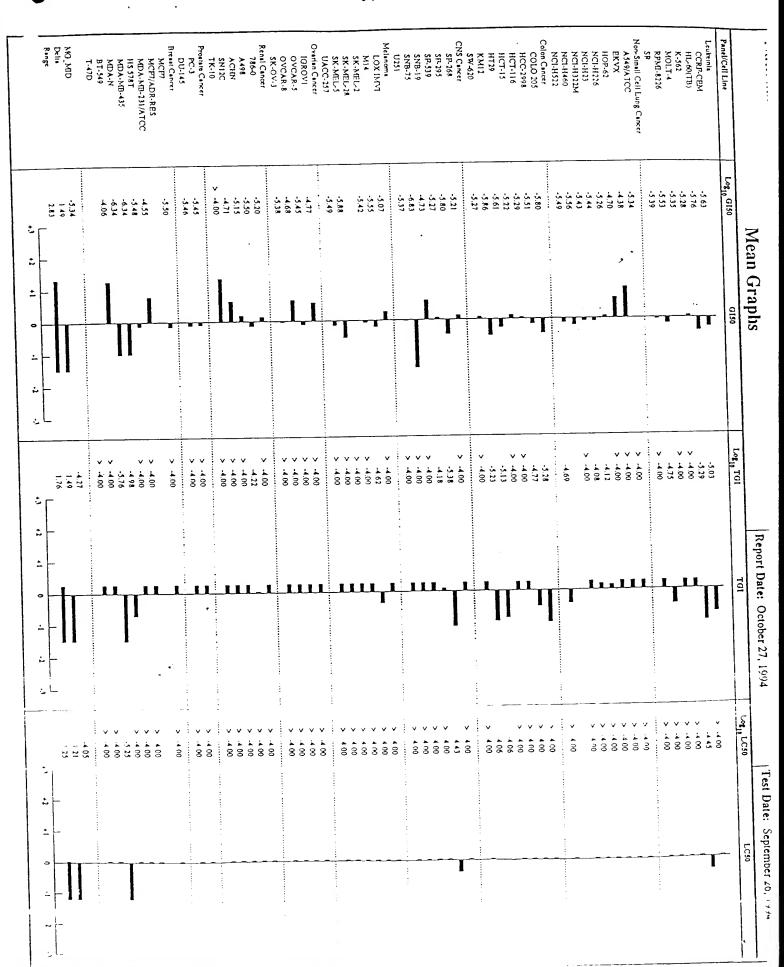
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279	7 4 (8) 9 10 10 10 10 10 10 10 10 10 10 10 10 10	363	7 4 5 5 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	3 2 3 3 3 3 5 5 5 5 5 5 5 5 5 5 5 5 5 5	300	7.7	0 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	3 17 3 28 3 28	\$ 12 \$ 23 \$ 23	.492 .535 .539	1 3 3 3	3 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2		\$ 3 3 3	3 X	5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	333	1.410 .
-		<u>'1 II</u>		և,		T	1	-11-	1	11-	11	1-11	7.1	L			Т	(1130
200	5.170 5.170 5.170 5.170 5.170 5.170	> 13 > 13 15 15 15	> 4.00 > 4.00	7.19.9 7.19.9 7.19.9 7.19.9	7.78 7.78 7.78 7.78	· · · · · · · · · · · · · · · · · · ·	> 400	2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	> 40	v v 1.3 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	× 488	> 4.00 2.00 2.00 2.00 2.00 2.00 2.00 2.00	3 A (0)	3 3 3 3 3 3 5 5 5 5 5 5 5 5 5 5 5 5 5 5	> 13 > 13	> 4 (8)	.4.42 -3.18 -4.49	Log <sub>10</sub> T(t)
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	> 1.03 2.13 3.03 3.03 3.03 3.03 3.03 3.03 3.03 3	333333		3 3 3 3 3 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	388	333	883	33838	87.4	3 = 88	333	8335	8 8 3 7 7 3	3388	98	388	338	Log <sub>10</sub> LC30
									:									1030

port Date: October 27, 1994 Test Date: September 26, 1994 QNS: MC:	C: D- 673162 -H / 0-1 / 2	Experiment ID: 9409SC89	Test Type: 8	Units: Molar
port Date. October 21, 11		Test Date: September 26, 1994	QNS:	MC:
MI: PHOMOPSIN A Stain Reagent: Dual-Pass SSPL: OFLC	port Date. October 27, 27		SSPL: 0FLC	

							Concentr	cation	Percer	ot Gra	net h				
	Time				l Densi		-4.0	-6.0 -	7.0 -	6.0 -	5.0 -	4.0	G150	TGI	LC 50
anel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	0.0							
æukemia	0.250	0.853	0.758	0.769	0.734	0.244	0.132	8 4	86	80		-47		9.40E-06 5.13E-06	
CCRF-CEM			0.679		0.686		0.073	75	88	, ,	-31 33	-65 11		>1.00E-04	
HL-60(TB) K-562							0.223	105 96	121 93	93 90	26	28	4.44E-06	>1.00E-04	1.00E-04
MOLT-4	0.281						0.560	103	94	67	9	-27	2.97E-06	1.78E-05	>1.00E-04
RPMI-8226						0.247	0.487	90	88	8.6	25	19	4.03E-06	>1.00E-04	-1.00E-04
SR			1.414	1.390	1.307	0.372	••••								.3 005 04
ion-Small Cell Lu	ng Cancer 0.361	1 608	1.696	1.649	1.386	0.762	0.678	107	103	82	34	25			>1.00E-04 >1.00E-04
A549/ATCC ERVX					1.562	1.239	1.117	107	99 114	92 99	56 57	45 35			>1.00E-04
HOP-62		1.643	1.641			1.293	1.114	100 87	85	96	34	-5	5.46E-06	7.59E-05	>1.00E-04
NC1-H226			0.924		0.961	0.720	0.564	101	101	88	20	-2	3.60E-06	8.30E-05	>1.00E-04
NCI-R23					1.417	0.765	0.899	93	93	80	27	44			>1.00E-04
NCI-H322M	0.556	1.332	1.277	1.049	0.913	0.324	0.235	101	95	80	12	_:	2.75E-06		>1.00E-04
NCI-H4 60	0.219 0.434	1.047	1.062	1.062	1.004	0.492	0.343	102	102	93	9	-21	3.27E-06	2.046-03	71.002-04
NCI-H522 Colon Cancer	0.434	1.04.							108	69	-27	-44	1.58E-06	5. Z4E-06	>1.00E-04
COLO 205	0.206	0.993	0.985	1.055	0.750	0.152	0.116 0.164	99 104	96	87	11	-37	3.09E-06	1.68E-05	>1.00E-04
HCC-2998	0.262	0.831	0.855	0.808	0.759 1. <b>4</b> 05	0.324		102	94	93	32	15	5.08E-06	>1.00E-04	>1.00E-04
HCT-116	0.230	1.467	1.507	1.415	2.910		1.035	102	99	103	35	15	6.07E-06	>1.00E-04	>1.00E-04
HCT-15	0.717	2.848 0.784	0.753	0.754	0.730	0.126	0.071	95	95	92	-14	-52	2.48E-06	7.39E-06	8.68E-05 6 8.72E-05
HT29	0.148	2.630	2.493	2.409	1.963	0.738	0.435	92	87	61	-19 34	-52 22	1.38E-06	31.00E-04	>1.00E-04
KH12 SW-620	0.140	0.747	0.774	0.773	0.703	0.349	0.274	104	104	93	34	22	•		
CNS Cancer							0.486	104	106	87	40	16	€.20E-0€	>1.00E-04	4 >1.00E-04
SF-268	0.367	1.090	1.120	1.132	0.994	0.660	0.258	100	94	74	-45	-53	1.59E-06	4.16E-0	6 3.70E-05
SF-295	0.554	1.306	1.303	1.263 1.568	1.526	0.844	0.481	99	102	98	32	-7	5.31E-06	6.61E-0	5 >1.00E-04
SF-539	0.517 0.587	1.546	1.539	1.709	1.662	1.231	0.961	101	98	94	56	33	1.85E-0	51.00E-0	4 >1.00E-04 4 >1.00E-04
SNB-19 SNB-75	0.367	C.848	0.767	0.629	0.502	0.440	0.444	63	55 98	28 91	15 26	16	4 23E-0	>1.00E-0	4 >1.00E-04
U251	0.191	0.840	0.862	0.830	0.781	0.357	0.247	103	98	91	26	-			
Helanoma					1.164	0.689	0.611	101	108	100	46	37	8.46E-0	5 >1.00E-0	4 >1.00E-04
IOX INVI	0.279	1.168	1.180		0.530	0.320	0.172	99	110	76	19	-31	2.82E-0	5 2.38E-0	5 >1.00E-04
M1.4	0.250 0.563	0.620	1.350		1.232	0.855	0.709	67	92	74	32	16	3.80E-0	5 >1.00E-0	4 >1.00E-04 4 >1.00E-04
SK-MEL-2 SK-MEL-28	0.305	0.827	0.804		0.664	0.496		96	98	69 54	37 22	51 10	1 325-0	6 >1.00E-0	4 >1.00E-04
SK-MEL-S	0.354	1.728	1.806		1.094	0.656		106 98	101 92	75	26	42	3.23E-0	6 >1.00E-0	4 >1.00E-04
UACC-257	0.709	1.849	1.826	1.759	1.565	1.004	1.189	90							
Owarian Cancer			1.490	1.646	1.535	0.968	0.646	104	119	109	57	27	1.70E-0	5 >1.00E-0	4 >1.00E-04
IGROVI	0.346	1.442	0.886			0.498		99	100	8.2	24	19	3.55E-0	6 >1.00E-0	4 >1.00E-04 4 >1.00E-04
OVCAR-5 OVCAR-8	0.550		2.538			1.674	1.121	105	133	104	59 26	30 47	2.09E-0	6 >1.00E-0	14 >1.00E-04
SK-OV-3	0.423		0.851	0.940	0.826	0.543	0.637	94	114	65	20	• ,			
Renal Cancer					1.865	0.988	0.686	91	97	98	38	17	6.30E-0	6 >1.00E-0	4 >1.00E-04
786-0	0.434							99	100	83	17	- 5	3.19E-0	6 6.00E-0	05 >1.00E-04
A498	0.561							98	90	90	43	21 28	7.03E-0	6 >1.00E-0	04 >1.00E-04 04 >1.00E-04
ACHN SN12C	0.636				1.627			105		103	59 92		>1.97E-0	4 >1.00E-0	04 >1.00E-04
TK-10	0.399	1.048	1.049	1.085	1.037	0.996	0.757	100	106	20	52	33			
Prostate Cancer					3.041	1.463	3 1.322	99	100	86	21	15	3.58E-0	6 >1.00E-0	04 >1.00E-04
PC-3	0.952							99	105	63	22	20	3.46E-0	6 >1.00E-	04 >1.00E-04
DO-145	0.459	1.630	1.61	1.000									2 125 /	AC 31 DOF-	04 >1.00E-04
Breast Cancer MCF7	0.259	1.241	1.22	4 1.244	1.009			96		76		12	3.13£-0	06 >1.00E-	
MCF7/ADR-RES			1.46	0 1.497				97		8 6 9 6		30	2.841-	05 >1.00E-	04 >1.00E-04
HOA-ME-131 A	mos c.e						• • • • • • • • • • • • • • • • • • • •					_	3.332 -	CE →1.00E-	64 →1.00E-04
HS 578T	0.58		1.27						81	34	1	-23	4.57E-	07 1.05E-	05 >1.00E-04
MDA-HIP-435	0.28		6 , 1.16 2   1.44			3 0.08	4 0.124	103		2.3			4 . 53E -	07 1.73E-	06 5.58E-06 04 >1 00F-04
MDA-N ·· BT-544	0.33 C.60					0.55	5 0.890		111		1.		b		02 31 00F=04
1-47b	6.77							•		•					

Report Date: October 27, 1994

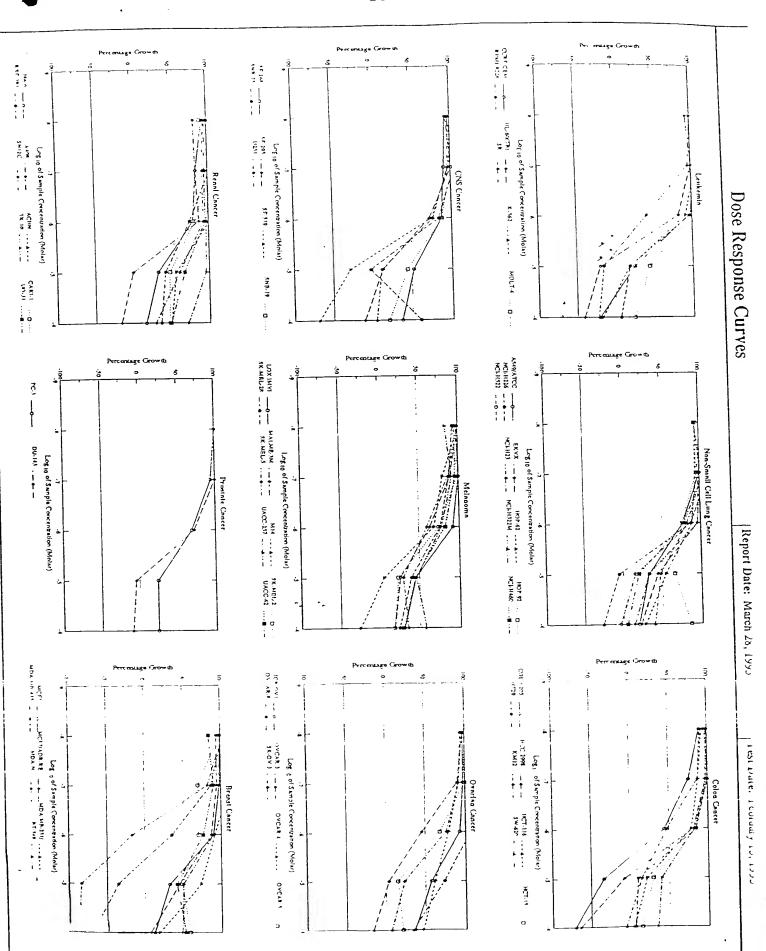
Test Date: September 26, 1994

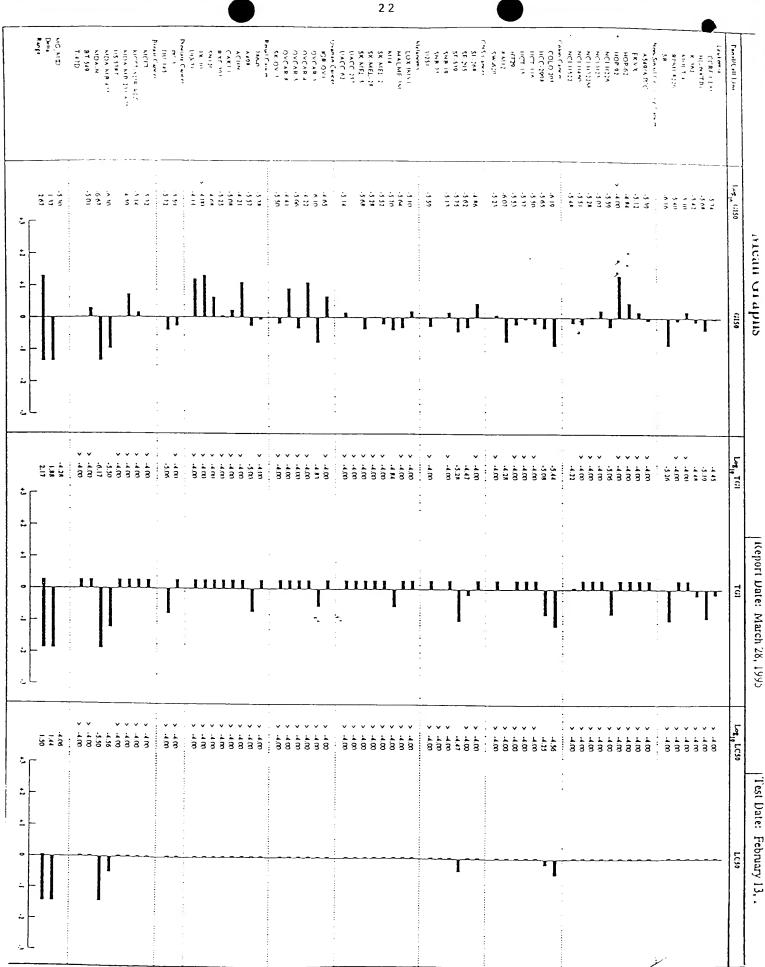


Experiment ID: 9502RM16 Test Type: 8 Units: Molar port Date: March 28, 1995 Test Date: February 13, 1995 QNS: SHP MC:

MI: Iso-phomopsin A Stain Reagent: Dual-Pass SSPL: 0FLC

							Concenti	at i on	_						
	Time			Optical	[Mensi	iles	-4.0	-6.0 -	Pe:ce			: . c	G150	TGI	1050
anel/Cell Line	Zero	Ctil -	- 0.9-	-7.0 -	€.0	- <b>5</b> . C	-4.0	-6.0	7.0						
eukemia	0.634	1.762	1.792	1.625 1			0.502	103	10€	97		-21 -41	4.54E-06	6 46E-06	>1.00E-04 >1.00E-04
CCRF-CEM NL-60 (TB)	0.592			1.622 1	.447		0.351	. e 2	100 104	63 92		-41 -17	3.76E-06	3.34E-05	>1.00E-04
K-562	0.362	1.370		1.411 1			0.317	100	100	101	44	24	7.96E-06	>1.00E-04	>1.00E-04
HOLT-4				1.647 1		1.201 0.696	0.788	110	110	57	19	6	4.02E-06	>1.00E-04	>1.00E-04
RPMI-6226	0.735 0.486			1.673 1 1.013 0		0.414	0.377	100	9€	41	-15	-22	6.95E-07	5.44E-06	>1.00E-04
SR :on-Small Cell Lur	U.486		1.031	1.015								16	4 115-06	>1 00F+04	1.00E-04
A549/ATCC	0.377	1.339				0.€92	0.556	104	100	77 96	33 44	3.5	7.61E-06	>1.00E-04	>1.00E-04
EKVX.						0.677 0.664	0.536 0.529	94	94	89	54	2.6	1.46E-05	>1.00E-04	>1.00E-04
HOP-62				0.663 C 1.101 I		0.004	1.066	96	Ģ€	76	66		>1.00E-04	>1.00E-04	>1.00E-04
HOP-92					0.634	0.573	0.446	114	110	3.8	-€	-27	2.55E-06	E. /3E-06	>1.00E-04 >1.00E-04
NCI-H226 NCI-H23	0.419			1.202	3 60 . 1	0.774	0.709	104	105	63	4 E 3 2	39 14	5.51E-06	>1 00E-04	>1.00E-04
NCI-H322H	0.624	1.566	1.627	1.551		0.926	0.752	106 93	96 105	96 79	20	4	3.27E-06	>1.00E-04	>1.00E-04
NCI-H460						0.393	0.228	101	97	66	15	-4	3.32E-06	6.00E-05	>1.00E-04
NCI-H522	0.413	1.073	1.081	1.050	0.992	0.314	0.555								
Colon Cancer	0.328	1.333	1.236	1.089	0.770	0.217	0.097	90	76	44	-34	-70			5 2.75E-05 5 5.66E-05
COLO 205 HCC-2996	0.590			1.246	1.142	0.545	0.214	9 E	97 6£	£2	−£ 21	-64 4	3.37E-06	>1.00E-04	>1.00E-04
HCT-116	0.161	1.304			1.0€1	0.406	0.211	93	96	ě5	29	14	4.23E-06	>1.00E-04	>1.00E-04
HCT-15	0.317				1.464 0.733	0.233	0.207	00	100	٤5	10	6	2.94E-06	>1.00E-04	>1.00E-04
HT29	0.166 0.294	0.631	0.824 1.343	1.296	C. 636	0.464	0.277	91	67	47	15	-6	6.55E-07	5.23E-0:	5 >1.00E-04 4 >1.00E-04
KM12 SW-620	0.156	0.691	0.670	0.667	0.766	0.450	0.410	97	99	€3	40	35	5.836-00	J1.00E-0.	71.002-01
CMS Cancer							0.617	94	92	8.6	52	37	1.365-05	>1.002-0	4 >1.00E-04
SF-266	0.463	1.431	1.373	1.352	1.314	0.966	0.356	95	100	73	12	-11	2 367-06	3.37E-0	5 >1.00E-04
SF-295	0.400	1.038	1.007		0.745	0.275	0.123	101	97	76	-29	-66	1.76E-06	5.28E-0	6 3.41E-05 4 >1.00E-04
SF-539 SNB-19	0,571	1.365	1.360	1.362	1.292		0.733	97	100	8 <u>9</u> 8 4	44 -3	20 60	7.37£-00	71.00E-0	>1.00E-04
SNB-75	0.361	0.626	0.619		382.0	0.370	0.529	97 96	104 96	77	11	4	2.552-06	>1.00E-0	4 >1.00E-04
U251	0.199	0.893	0.576	0.867	0.736	0.276	0.226	50	,,,	• •					
Hel anoma	0.191	0.962	0,963	0.980	0.921	0.551	0.430	96		92	45	30	6.C1E-06	>1.00E-0	4 >1.00E-04 4 >1.00E-04
LOX IMVI MALME-3H	0.464	1.037	1.039	0.976	0.631	0.611		100			26 5	17 -26	1.98706	1.45E-0	5 >1.00E-04
M14	0.196	0.569	0.571	0.496	0.453	0.215		101 94		75	23	17	3.C1E-06	>1.00E-0	4 >1.00E-04
SK-MEL-2	0.746	1.368	1.331	1.360	1.212	0.667		93		77	40	24	5.22E-0	>1.00E-0	4 >1.00E-04
SK-MEL-26	0.576	1.166	1.146	1.114	0.622	0.320	0.375	66			29	35	2.11E-0	>1.00E-0	4 >1.00E-04 4 >1.00E-04
SK-MEL-5 UACC-257	0.034		1.175	1.234	1.133	0.885		64			46 45	56 29	7 21 == 0	5 >1.00E-0	4 >1.00E-04
TACC-62	0.577	1.662	1.808	1.610	1.639	1.150	0.946	è 6	96	63	• •				
Ovarian Cancer					1.605	1.192	0.937	9.6	97	93	56	36	2.16E-C	5 >1.00E-0	04 >1.00E-04
IGR-OV1	0.515		1.661 0.886	1.656 0.646	0.572	0.314	0.244	ō-7				-17	7.97E-C	7 1.4/2-0	05 >1.00E-04 04 >1.00E-04
OVCAR-3 OVCAR-4	0.467		1.151	1.121	1.026	0.906	0.798	9.7				47 21	2 207-0	6 >1.00E-0	04 >1.00E-04
OVCAR-5	0.393		0.672	0.684	0.730	0.467		100				34	3 63F-0	5 >1.00E-0	04 >1.00E-04
OVCAR-6	0.267		1.256		1.252	0.950		9				6	3.135-0	6 >1.00E-	04 >1.00E-04
SK-OV-3	0.468	1.011	0.962	0.966	0.662	0.000		_						6 N 00F~	04 >1.00E-04
Renal Cancer 766-0	0.200	0.949	0.901	0.629	0.794	0.442	0.317	9.	-			16 -16	2 477-0	6 0 04F	06 >1.00E-04
A496	1.061	1.413	1.354	1.359	1.371	1.079	0.903	δ. 10				4.5	6 33F-0	5 >1.00E-	04 >1.00E-04
ACHN	0.406				1.470 0.862		5 0.690	9				<b>4</b> 6	1 777-0	6 >1.00E-	04 >1.008-04
CAKI-1	0.466				1.361		0 1.013	10					5.591-0	6 >1.00E-	04 >1.00E-04 04 >1.00E-04
RXF-393 SN12C	0.704				1.270	0.95	5 0.640	9					>1 DOE-0	04 >1.00E-	04 >1.006-04
TK-10	0.62			1.113	1.076	1.07		10					7.E1E-0	5 >1.00E-	04 >1.00E-04
00-31	0.593	3 1.476	1.452	1.440	1.439	1.16	6 1.016		,	•	•				
Prostate Cancer	0.30	2 1.164	1.161	1.115	0.893	0.50	4 0.503	10					2.562-	06 >1.00E-	04 >1.00E-04 -06 >1.00E-04
PC-3 DU-145	0.33		1.077	1.026				10	7 10	0 7	2 -5	- <del>-</del> •			
Breast Cancer									, o o	8 9	o 32	1.2	4.845-	06 >1.00E-	-04 >1.00E-04
HCF7		3 Z.139		1.123		C.64	9 0.509 0 0.37E	-		5 6	7 44	. 7			
MCF7/ADR-RES		0 1.03			0.66	6 0.78	6 0.502		7 11				2.60E-		-04 >1.00E-04 -04 >1.00E-04
MDA-ME-231/F HS 578T	0.86					€ 1.11	9 1.174				0 40			07 3 13E-	-06 2.76E-US
MDA-MB-435	0.32	0 1.26	6 1.31	4 1.164	0.€5	3 C.20	0.095			57 3 52 <b>-</b> 1	•			a- C 635.	-07 3.16E-06
MDA-N	0.21				0.:-	9 C.03			-	e 9	0 5	0 46	9.72E-	06 >1.00E	-04 >1.00E-04
BT-549	0.47		6 0.51	5 0.600 7 2.015						0 7	6 4	1 52	:	. >1.00E	-04 >1.00E-04
T-47D	0.71	. 4.13	J 1.72	. 2.01-											





· D. 3164 - J / 0-1 / 4	Experiment ID: 9409SC89	Test Type: 8	Units: Molar
	Test Date: September 26, 1994	QNS:	MC:
	Stain Reagent: Dual-Pass	SSPL: OFLC	

							Concent	ration			out h				
	Time				l Densi	ties		-6.0 -	Perce			4 0	GI 50	TGI	LCSO
el/Cell Line	Zero	Ctil	-8.0	-7.0	-6.0	-5.0	-4.0	-6.0 -	7.0 -	C. 0 -	5.0	•	010-		
kemia					0.799	0.292	0.143	103	97	92	7	-43	3.12E-06	1.36E-05	>1.00E-04
CCRF-CEM		• • • • •					0.086	106	9.6		-29	-59		5.69E-06	
HL-60 (TB)							0.159	126	123	112	25	5	5.16E-0€	>1.00E-04	1.00E-04
K-562							0.327	97	105	106	46	5		:1.00E-04	
HOLT-4						0.196	0.168		104	67	0	-14			1.00E-04
RPMI-8226				1.544	1.488	0.609	0.307	è 6	òċ	94	26	5	4.6/1-06	>1.00E-04	.1.00E-04
SR 1-Small Cell Lur									103	90	31	11	4 76F-06	>1.00E-04	1.00E-04
AS49/ATCC	0.361	1.402					0.476		102	98	64	58	>1.00E-04		
EKVX				1.712			1.279	95	62	79	53	21	1.21E-05	>1.00E-04	1.00E-04
HOP-62				1.579	1.546 0.963		0.500	95	93	110	39	-15			1.00E-04
NC1-H226	0.591			0.906 1.630	1.493	0.875	0.636		105	93	37	16	5.93E-06		1.00E-04
NCI-H23	0.455	1.575		1.395	1.267	0.840	0.986	95	100	€5	34	51	•		1.00E-04
NCI-H322M	0.556			1.025	0.940	0.281	0.150	95	9€	€5	7	-32	2.84E-06		>1.00E-04
NCI-H460	0.434	1.065		1.059	1.034	0.500	0.104	100	50	<u>9</u> 5	10	-7 ü	3.40E-06	1.321-05	5.00E-05
NCI-H522 lon Cancer	0.434	1.000										-48	2 645-06	4 245-06	>1.00E-04
COLO 205	0.206	0.975	0.991	1.024	0.792	0.114	0.109	102	10€	76 92	-45 15	-35	3 55E-06	2.03E-05	>1.00E-04
HCC-2998	0.262	0.673	0.848	0.866	0.826	0.356	0.171	96	111	92	30	-55			>1.00E-04
HCT-116	0.230	1.417	1.419	1.549	1.405	0.583	0.300 1.050	100 100	102	102	40	16			>1.00E-04
HCT-15	0.717	2.647	2.851	2.880	2.893	1.573	0.110	98	96	93	-30	-26	2.24E-06	5.68E-06	>1.00E-04
HT29	0.145	0.617	0.806	0.804	0.774	0.611	0.283	116	98	62	-33	-69	1.35E-06	4.53E-06	3_02E-05
IO41.2	0.907	1.983	2.156 0.683	0.687	0.618	0.269	0.149	99	99	87	23	2	3.82E-06	>1.00E-04	>1.00E-04
SW-620	0.140	0.690	0.663	0.007	0.010	0.202									×1 00E-04
S Cancer	0.367	1.294	1.313	1,235	1.173	0.792	0.651	102	94	67	46	31	7.91E-06	>1.00E-04	>1.00E-04 7.57E-05
SF-268 SF-295	0.554	1.239	1.239	1.193	1.158	0.354	0.267	100	93	88	-36	-52 6	2.036-06	3.12E-06	>1.00E-04
SF-233	0.517	1.466	1.449	1.435	1.309	0.789	0.576	96	95 98	€2 89	28 57	37	2 34F-05	>1.00E-04	>1.00E-04
SNB-19	0.567	1.709	1.709	1.684	1.590	1.230	1.007	100 84	102	106	23	36	4.72E-06	>1.00E-04	>1.00E-04
SNB-75	0.367	0.601	0.730	0.810	0.627	0.466	0.523	97	93	63	15	-20			>1.00E-04
<del>02</del> 51	0.191	0.€74	0.852	0.829	0.755	0.293	0.152			0.5					
·l anoma				1,108	1.061	0.653	0.444	99	9€	91	43	19			>1.00E-04
LOX IMVI	0.279	1.142	1.136	0.456	0.370	0.235	0.106	76	€1	46	-6	-56			7.13E-05
161.4	0.250	1.347	1.349	1.305	1.191	0.705	0.566	100	55	80	16	O	3.06E-06	>1.00E-04	>1.00E-04
SK-MEL-2	0.305	0.940	0.894	0.906	0.800	0.602	0.577	93	95	78	47	43	7.89E-06		>1.00E-04 >1.00E-04
SK-MEL-26 SK-MEL-5	0.354	1.476	1.666	1.591	0.613	0.347	0.370	117	110	41 85	-2 20	1 27			1 >1.00E-04
UACC-257	0.709	1.939	1.918	1.889	1.751	0.960	1.035	98	9€	83	20	21	J.402 00		
rarian Cancer							0.660	105	10€	94	49	27	9.72E-0	>1.00E-0	4 >1.00E-04
IGROV1	0.346	1.494	1.546	1.561	1.429	0.914	0.523	102	100	95	30	25	4.87E-0	>1.00E-0	4 >1.00E-04
OVCAR-5	0.377	0.957	0.970	0.954	2.718	1.919	1.214	103	107	105	66	32	2.95E-C	>1.00E-0	4 >1.00E-04
OVCAR-8	0.550	2.624 C.662	2.695 0.882	0.666	0.802	0.530	0.576	105	10€	86	24	3.5	3.86E-0	>1.00E-0	4 >1.00E-04
SK-OV-3	0.423	0.002	0.002	0.000	••••								6 005 0	1 005-0	4 >1.00E-04
enal Cancer 786-0	C.434	1.823	1.726	1.743	1.613	0.992	0.760	93	94	99	40	24	6.8ZE~0	5 31.00E-0	4 >1.00E-04
A498	0.561		0.908	0.893	0.901	0.634	0.572	97	93	95	21 46	3 21	£ 02E-0	5 >1 00E-0	4 >1.00E-04
ACHN	0.306		1.181	1.125	1.087	0.701	0.467	101 102	6 č	91 101	€5	24	2.36E-0	5 >1.00E-0	4 >1.00E-04
SNI 2C	0.636	1.662		1.655	1.676	1.306	0.884	101	103	101	67	5.8	>1.00E-0	>1.00E-0	4 >1.00E-04
TK-10	0.399	1.066	1.072	1.090	1.072	0.981	0.789	101	102						
rostate Cancer				3.498	2.967	1.625	1.382	101	10€	ε5	28	18	4.11E-0	6 >1.00E-0	4 >1.00E-04
PC-3	0.952		3.364 1.627					106		97	16	5	3.77E-0	6 >1.00E-0	4 >1.00E-04
DO-145	0.459	1.560	1.027	1.070	1.520										4 >1.00E-04
reast Cancer	0.259	1.163	1.204	1.109	0.900	0.442	0.291	102		69	20	3	2.46E-0	6 31.00E-0	4 >1.00E-04
MCF7/ADR-RES	0.233					0.670				95		2 26	3.90E-0	5 >1.00E-0	4 >1.00E-04
MDA-MB-231/AT				1.663		1.286							4.03F-0	6 >1.00E-0	4 >1.00E-04
HS 578T	0.586	1.116	1:132			0.786							1.25E-0	6 .	>1.00E-04
MDA-MB-435	0.283		. 1.185	1.255						_			6.90E-0	7 7.30E-0	6 >1.00E-04
MDA-N	0.332											32	3.44E-0	5 >1.00E-0	4 >1.00E-04
BT-549	0.606										_		7.46E-0	€ >1.00E-0	4 >1.00E-04
T-47D	0.775	2.137	2.196	2.079	2.1/4	1.333	1.552								

Dose Response Curves

Report Date: October 27, 1994

Test Date: September 20, 1994

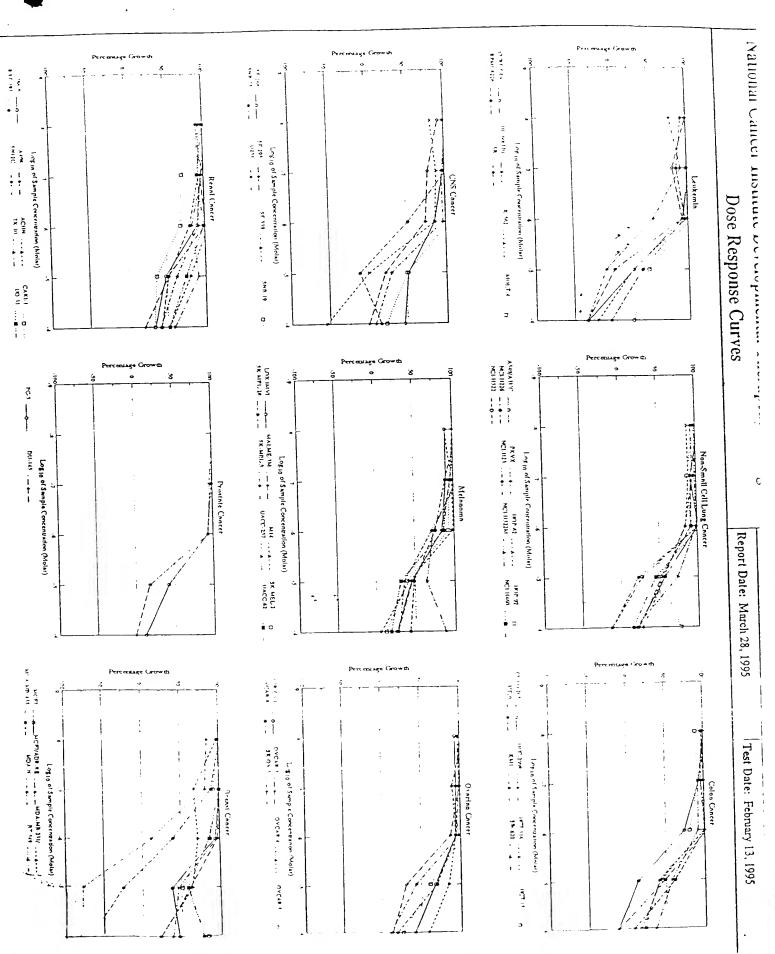
0150 Log <sub>0</sub> TOI	MO_MID Delia P-:-ge	MDA-MB-433 MDA-N BT-549 T-47D	Breat Cancer MCF7 MCF7/ADR-RES MDA-MB-231/ATCC HS 578T	Prosible Cancer PC-3 DU-145	Renal Cancer 786-0 A498 ACHOV SV12C TX-10	Ovarian Career IOROV1 OVCAR-5 OVCAR-8 SK-OV-3	Melanoma MIA MIA SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-5 UACC-257	CNS Cancer SP-268 SP-295 SP-539 SP-539 SNB-19 SNB-19 U251	Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HT79 KMI2 SW-620	Non-Small Cell Lung Caccer A549/ATCC EKVX HOP-62 NCI-H226 NCI-H23 NCI-H23 NCI-H260 NCI-H260	Leukemia CCRP-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	Penel/Cell Line
Leg <sub>0</sub> TOI  Leg <sub>0</sub>	-5 29 0.87 2.16	3.13	5.61 5.46 5.39	.5.39 -5.42		-5.01 -5.31 -4.53	-5.14 -6.10 -5.51 -5.10 -6.13	-5.10 -5.69 -5.41 -6.33 -5.53	-5.79 -5.45 -5.29 -5.16 -5.65 -5.67 -5.42	> 4.00 > 4.00 -4.92 -5.115 -5.23 -5.23 -5.23	.5.51 .5.62 .5.29 .5.06 .5.57	
	÷ [	1	V V V V V V V V V V V V V V V V V V V	> .4.00 > .4.00	0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.0	807 × × × × × × × × × × × × × × × × × × ×	× + 100 × + 100 × + 100 × + 100	> 4.00 > 4.00 > 4.00 > 4.00 > 4.58	-5.37 > -4.69 > -4.00 > -4.00 > -5.25 > -5.24 > -4.00		-4.86 -5.23 -4.00 -4.00 -4.98 -4.00	
and the contract of the contra	1	> 400 > 400	/ / v v v	> 400	> 400 > 400 > 400	V 100 V 100 V 100 V 100	× 4.39 × 5.39 × 5.30 ×	.412 >.400 >.400 >.400 >.400 >.400	> 1.00 > 1.00 > 1.00 > 1.00 > 1.00 > 1.00 > 1.00	V	V 1.00 V	

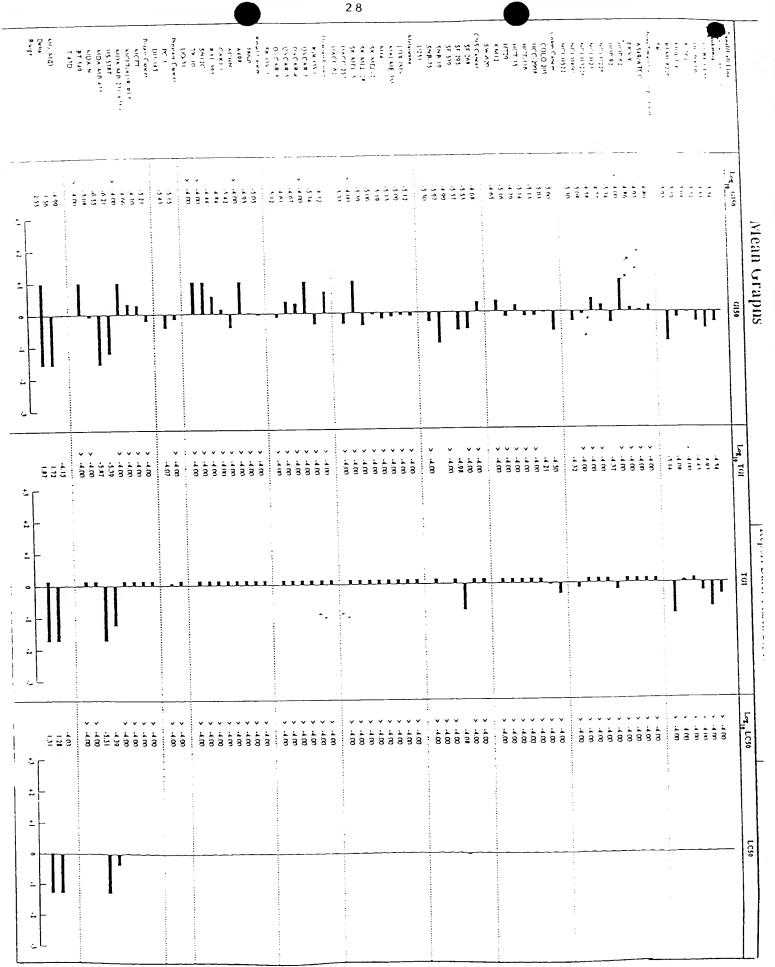
Experiment ID: 9502RM16 Test Type: 8 Units: Molar

port Date: March 28, 1908 Test Date: February 13, 1905 QNS: SHP MC:

DMI: Octahydrophomopsin A Stain Reagent: Dual-Pass SSPL: 0FLC

							Concentr	ation	Perce	nt G:	ひゃてた				
	Time Zero	Ctil		Optical -7.0 -		-5.0	-4.C	- 6 . C -				c	<b>51</b> 50	7.11	ಎ೯೬೯
Panel/Cell Line	26.0							0.0		93	26 -	. 3 3	4.611-06		+1.00E-04
CCRF-CEM			1.656	1.663			0.423	100	102 £1	93		-34	2.968-06	1.171-13	11.00E-64 >1.00E-04
HL-60 (TB)						0.608	0.303		100	ç ç		- 2 1			
K-562 HOLT-4			1.766			1.196	0.966	104		103	46	2 €			>1.00E-04 >1.00E-04
RPMI-6226		1.450	1.406	1.355		1.015	0.711	94 76	67 92	96 54	3º .	-3 -25	1.161-06		>1.00E-04
SR	0.486		0.776	0.627	0.686	0.444	0.318	76	72	J.	-,				
Non-Small Cell Lu	ng Cancer 0.377	1 362	1.405	1.289	1.366	0.942	0.579	104	<u>9</u> 3	101	57	213	1.59E-C5	91.51E-14	>2.00E-04
A549/ATCC EKVX			0.961	0.896	0.695	0.680	0.523	105	93	93	5.2	23 21			.1.00E-04 >1.00E-04
HOF-62	0.391					0.699	0.507	é è E è	90 66	₽5 92	55 51		>1.00E-04		
HOP-92						0.671	0.524		104	102		-14	4.52E-06	4.00E-05	>1.00E-04
NCI-H226 NCI-H23	0.607 0.419					0.664	0.634	94	96	€ 5	57	27	1.66E-C5	>1.01E-04	>1.00E-04
NCI-R23		1.629	1.615	1.607	1.616	1.368	0.799	99	9.6	99	74 45	17			>1.00E-04 >1.00E-04
NCI-H460						0.609	0.319 0.360	105 106	101 103	104		-13			>1.00E-04
NCI-H522	0.413	0.954	1.000	0.969	0.965	0.561	0.360	100	103		_	••			
Colon Cancer COLO 205	0.326	1.242	1.250	1.163	1.006		0.285	101	94	74		-13			>1.00E-04
HCC-2998	0.590	1.321	1.301			0.944		97 105	100	104	46 42	-13 27			>1.00E-04 >1.00E-04
HCT-116	0.161						0.341	90	9-3	161	45	22			>1.00E-04
HCT-15	0.317	1.751 0.659	1.602 0.640			0.592	0.219	97	96	101	61	8			>1.00E-04
HT29 KM12	0.294	1.232	1.237		1.227	0.672	0.484	101	96	ه د	40	20	6.662-06	>1.CTE-04	>1.00E-04 >1.00E-04
SW-620	0.156	1.016	1.016	0.955	0.947	0.652	0.466	100	93	92	56	36	2.242-03	71.012-04	71.00L-04
OIS Cancer			3 300	1.262	1.166	0.696	0.647	101	96	86	52	46	2.07E-05	>1.01E-04	>1.00E-04
SF-268 SF-295	0.463	1.301	1.309		0.903	0.551	0.401	93	79	74	22	0	2.94E-06	>1.01E-04	>1.00E-04
SF-539	0.367	0.866	0.802	0.833	0.619	0.393	0.176	63	90	67 104	1 50	-55 23	2.665-06	1.03E-03	6.29E-05 3 >1.00E-04
SNB-19	0.571	1.452	1.464	1.461		1.013	0.769 0.420	101	103	52	-11	16	1.06E-06	-	>1.00E-04
SNE-75	0.361	0.628 0.851	0.626 0.868	0.633 0.625		0.341	0.255	103	96	97	30	9	5.02E-06	>1.E:E-C4	>1.00E-04
U251 Helanoma	0.199	0.631	0.800	0.015								2.5	7 (45 06	>: c:==0:	>1.00E-04
LOX INVI		1.076	0.996	0.997		0.593	0.416 0.594	91 00	91 91	65 64	45 46	25 27	E. 09E-06	>1.00E-04	>1.00E-04
HALME-3M	0.464	0.952	0.949	0.934 0.521	0.677	0.691	0.394	90	36	96	43	5	7.35E-06	>1. CCE-04	>1.00E-04
M14 SK-MEL-2		0.527	1.408	1.377	1.356	1.007	0.624	101	96	93	40	12	6.41E-06	>1.00E-0	>1.00E-04
SK-MEL-28		1.271	1.313	1.201	1.106	0.913	0.675	106	90 107	76 72	46 36	43 26	£.11E-06	>1 DCE-0	<pre>4 &gt;1.00E+04 5 &gt;1.00E-04</pre>
SK-MEL-5	0.034	1.051	1.156	1.123	0.765	0.402	0.319 1.057	110	105	74	65	66	>1.00E-04	>1.00E-0	4 >1.00E-04
UACC-257	0.536		1.159	1.155	1.633	0.959		104	96	67	31	16	4.€5E-06	>1.005-0	4 >1.00E-04
UACC-62 Ovarian Cancer	0.377	1.720	1.050	22.727									4 7:- 05	S1 515-0	4 >1.00E-04
IGR-OV1	0.515	1.761	1.668	1.697	1.663	1.362	1.032	94 103	9 S	94 87	6E 31	42 13	4.57E-06	>1.00E-0	4 >1.00E-04
OVCAR-3	0.293		0.625	0.806	0.745	0.452		106	90	94	€5	50	>1 007-04	>1.00E-0	4 >1.00E-04
OVCAR-4 OVCAR-5	0.467		0.893	0.882	0.667	0.662		107	104	105	62	26	2.122-05	>1.002-0	4 >1.00E-04 4 >1.00E-04
OVCAR-6	0.267	0.947	0.932	0.937	0.911	0.743		39	60 66	95 96	70 43	19	7.58E-06	>1.03E-0	4 >1.00E-04
SK-OV-3	0.468	0.975	0.994	0.923	0.965	0.666	0.519	104	90	3.0	4.5	10			
Kenzl Cancer 766-0	0.200	0.913	1.003	0.888	0.844	0.543	0.436	113			46	33	9.01E-06	>1.CE-0	4 >1.00E-04
786-0 A496	1.081			1.546	1.5€9	1.331	1.179	104			51 61	20 5.2	1.112-05	) >1.00±~0   >1.50F~0	4 >1.00E-04 4 >1.00E-04
ACHN	0.406			1.430	1.436	1.206		100 95			36	32	3.772-06	5 >1.ECE-0	4 >1.00E-04
CAKI-1	0.466				0.792	0.636		ءَ وَ			52	42	1.44E-05	>1.tGE-0	4 >1.00E-04
RYF-393 SN12C	0.704				1.201	0.936		91			63	40	3.67Z-0	5 >1.00E-0	34 >1.00E-04 34 >1.00E-04
TK-10	0.627	1.221	1.172	1.207	1.122	1.167		92 100			91 75	59 52	>1.00E-0	>1.03E-0	4 >1.00E-04
00-31	0.593	1.442	.1.440	1.370	1.431	1.228	1.030	100	52	. 55	.,				
Prostate Cancer	0.302	1 006	1.130	1.086	1 042	0.636	0.395	104	99	93	42	12	7.00E-0	6 >1.0E-0	24 >1.00E-04
PC-3 DU-145		1.061		1.036	1.016			100	97	94	17	- 1	3.75E-0	6 E.SUE-4	5 >1.00E-04
Breast Cancer								104	100	94	36	46	6.125-0	6 >1.1CE-	04 >1.00E-04
MCF7	0.423	3 .1.174 0.907	1.207					102			61	23	1.967-0	5 >1.00E-0	C4 >1.00E-04
MCF7/ADR-RES MDA-MB-231/A							0.529	ō-	7 67		64	22	2.165-0	5 >1.1CE-	04 >1.00E-04 C4 >1.00E-04
HS STET	0.66	4 1.319	1.334	1.282	1.261	1.09		103		_	51 - 25	63 -66	>1.00E-0 6.22E+0	7 4.19E-	06 4.05E-05
MDA-ME-435	0.32							101 E				-60	2 807-0	7 1.34E-	C6 4.94E-06
MDA-N BI-549	0.21							12	3 10	€ 96	46	36	E.41E-0	6 >1.:CE-	04 >1.00E-04
T-47D	0.71		2 1.984					9	10 ء	0 66	59	77	>1.00E-0	4 >1.10E-	04 >1.00E-04





: D- 673163 -1 / 0-1 / 3	Experiment ID: 9409SC89	Test Type: 8	Units: Molar
rt Date: October 27, 1994	Test Date: September 26, 1994	QNS:	MC:
n: octahydrophomopsin a	Stain Reagent: Dual-Pass	SSPL: 0FLC	

						X 10									
	Time		Mea	n Optic	al Dens		Concent	.I ac I on	Perce	ent Gr	owth				
el/Cell Line	Zero	Ctrl	-6.0	-7.0	-6.0	-5.0	-4.0	-6.0				-4.0	GI 50	TGI	1.050
kemia												_			
CCRF-CEM	0.250	0.846	0.785	0.823	0.736	0.301		90	96 95	82 88	6 -25	-3 -49	2.71E-06		>1.00E-04 >1.00E-04
HL-60 (TB)	0.213	0.710	0.741	0.686	0.649	0.160	0.109	106 100	106	92	22	14			>1.00E-04 >1.00E-04
K-562	0.129	0.726	0.727 1.167	0.774	0.682	0.261	0.215	103	112	105	39	20			>1.00E-04
MOLT-4	0.281 0.196	0.784	0.841	0.776	0.692	0.239	0.131	110	00	84	7	-33			>1.00E-04
RPHI-8226		1.562	1.483	1.509	1.456	0.600	0.432	94	é é	92	27	15			>1.00E-04
SR -Small Cell Lui			1.405	1.505	1.150						_				
A549/ATCC	0.361	1.402	1.450	1.442	1.370	0.849	0.507	105	104	97	47	14			>1.00E-04
EKVX	0.686	1.701	1.649	1.673	1.583	1.317	1.133	95	97	88	62	44			>1.00E-04
HOP-62	0.834	1.738	1.762	1.704	1.779	1.486	1.222	103	9€	105	72	43			>1.00E-04
NCI-H226	0.591	0.929	0.879	0.843	0.876	0.702	0.461	85	75	85	33	-22			>1.00E-04
NCI-H23	0.455	1.575	1.684	1.778	1.623	1.229	0.593	110	116	104 91	69 49	12 26			>1.00E-04 >1.00E-04
NCI-H322M	0.556	1.391		1.383	1.313	0.969	0.775	100	99	96	29	2			>1.00E-04
NCI-H460	0.219	1.062	1.058	1.051	1.028	0.462	0.239 0.468	99	95	88	23	5			>1.00E-04
NCI-H522	0.434	1.065	1.059	1.059	0.992	0.435	U.468	22	2.2	00	•	,	0.402-00	>1.00L-04	71.002-04
on Cancer	0.208	0.975	0.956	0.972	0.745	0.216	0.037	97	100	70	1	-67	1.95E-06	1.03E-05	4.11E-05
COLO 205	0.262	0.873	1.115	1.211	1.084	0.687	0.221			135		-16	1.33E-05	6.16E-05	>1.00E-04
HCC-2996 HCT-116	0.230	1.417	1.467	1.447	1.413	0.721	0.392	104	103	100	41	14	7.11E-06	>1.00E-04	>1.00E-04
HCT-115	0.717	2.847		2.780	2.787	1.946	1.060	96	97	97	5.8	2 €	1.53E-05	>1.00E-04	>1.00E-04
HT29	0.148	0.817	0.772	0.755	0.749	0.351	0.191	93	Ē.	90	30	€.			>1.00E-04
KM12	0.907	1.983	2.068	2.236	2.404	1.586	0.833	108	124	139	63	-6			>1.00E-04
SH-620	0.140	0.690	0.664	0.678	0.618	0.325	0.319	95	36	87	34	32	4.92E-06	>1.00E-04	>1.00E-04
Cancer			_				. :		100	0.0	43	22	6 705-06	>1 005-04	>1.00E-04
SF-268	0.367	1.294		1.290	1.161	0.764	0.572	101 88	100 88	86 72	-27	-65	1.67E-06		4.04E-05
SF-295	0.554	1.239	1.154	1.158	1.048	0.405 0.780	0.194	101	95	95	27	-32	4.62E-06		>1.00E-04
SF-539	0.517	1.486	1.496	1.437	1.440	1.254	1.014	100	97	99	59	38			>1.00E-04
SNB-19	0.587	0.801	0.757	0.850	0.753	0.342	0.483	90	111	89	-7	27	2.55E-06		>1.00E-04
SNB-75 0251	0.191	0.874	0.848	0.869	0.806	0.327	0.185	96	9.5	90	20	- 3	3.72E-06	7.30E-05	>1.00E-04
anoma	0.151	0.0.4	0.010	••••											
LOX IMVI	0.279	1.142	1.113	1.138	1.069	0.724	0.617	97	100	92	52	39			>1.00E-04
M1.4	0.250	0.509	0.510	0.431	0.493	0.313	0.122	101	70	94	24	-51	4.27E-06		9.70E-05
SK-MEL-2	0.563	1.347	1.436	1.420	1.391	0.858	1.033	111	106	106	36	60			>1.00E-04
SK-MEL-28	0.305	0.940	0.972	0.901	0.743	0.489	0.564	105	94	69 45	29 3	41 -19			\$ >1.00E-04 5 >1.00E-04
SK-MEL-5	0.354			1.533	0.864	0.388	0.287	93 96	105	85	36	37			>1.00E-04
<b>TACC-257</b>	0.709	1.939	1.910	1.898	1.755	1.149	1.159	96	٠, و	63	36	٠, د	2.14E-00	, >1.00E-0.	71.00L-04
rian Cancer	0 246	1.494	1.567	1.579	1.480	0.947	0.733	108	107	99	52	34	1.35E-05	>1.00E-0	4 >1.00E-04
IGROVI OVCAR-5	0.346	0.957	0.968	0.921	0.933	0.710	0.518	102	94	96	57	24			4 >1.00E-04
OVCAR-5 OVCAR-8	0.550			2.595	2.626	1.832	1.160	106	9.9	100	62	29	2.32E-05	>1.00E-0	4 >1.00E-04
SK-OV-3	0.423			0.851	0.770	0.543	0.377	€5	9€	79	27	-11	3.63E-06	5.21E-0	5 >1.00E-04
nal Cancer															
786-0	0.434	1.623	1.873	1.963	2.204		1.181	104	110	127	95	54			4 >1.00E-04
A498	0.561			0.917			0.617	104	100	103	49	16			4 >1.00E-04
ACHN	0.306			1.138		0.830	0.495	99	96	86 92	61 63	22 26			4 >1.00E-04 4 >1.00E-04
SN12C	0.636			1.625		1.283	0.924	99 97	6.€ ق.€	101	87	51			4 >1.00E-04
TK-10	0.399	1.048	1.047	1.042	1.073	0.980	0.739	91	-6	101	67		>2.00E-04	. >1.00L-0	71.002.01
ostate Cancer	0.050	2 263	3 063	3,359	3.104	1.852	7 447	ро	100	90	37	21	5.76E-06	5 >1.00E-0	4 >1.00E-04
PC 3	0.459			1.654				105	108	9.5	19	- 4	4.77E-06	5 7.50E-C	5 74.00E-04
DO-145 Past Cancer	0.439	1.560	1.010	1.054	1.550	00									
MCF7	0.259	1.183	1.323	1.253	1,261	0.576	0.498	115	106	108	34	2 €			4 >1.00E-04
MCE // Aut = tau	. 52.		1.32	1.351	1.341	1.536		107	:	205	e e	7 5	•		e ≈s vô£-vi
MDA-ME-231/AT					1 482					€ 3	50	2.3			4 (1.00E-04
HS 578T	0.586							90		72	13	-10	2.37E-0		5 >1.00E-04
HDA-HB-435	0.283							100		59	13	-14	1.58E-0		5 >1.00E-04 € ≥1.00E-04
MDA-N	0.332							101		51 67	- 9 57	ئيز - 37	1.02E-0		4 >1.00E-04
BT-549	0.606							111 95		89	45	48			4 >1.00E-04
T-47D	0.775	2.137	2.071	2.441	1.986	1.393	1.431	32	122	0 9		70	L-0	<b> </b>	

Dose Response Curves

Report Date: October 21, 1994

I est Date. September 20, 1977

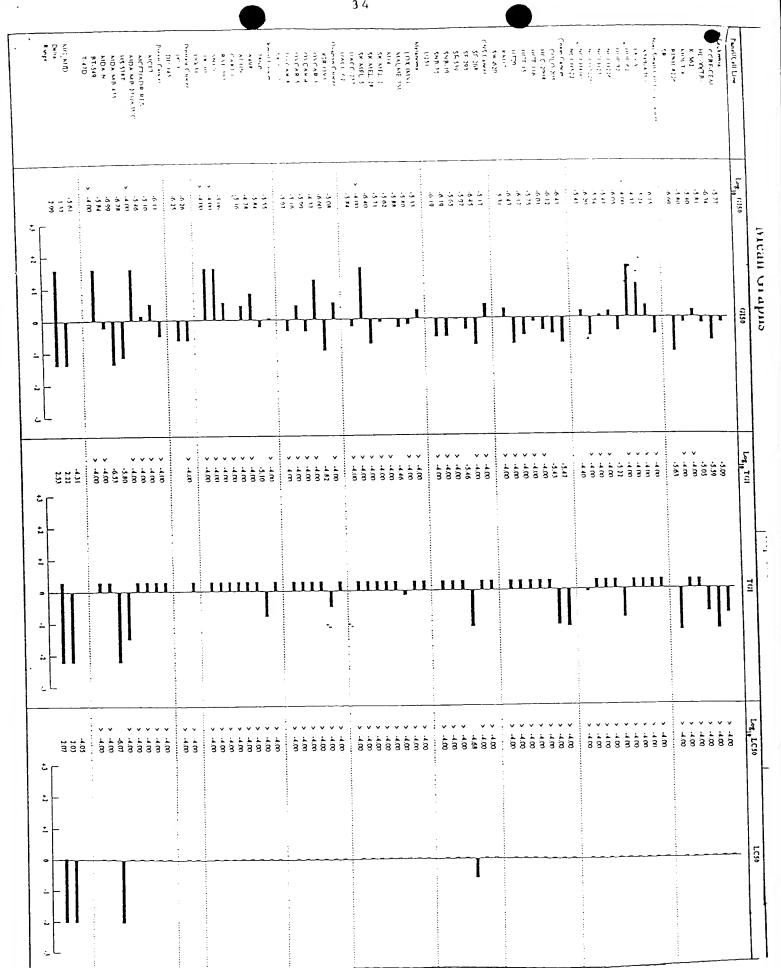
Delta Range	1 1 2	MDA-N BT-549	MDA-MB-435	MDA-MB-231/ATCC	MCFI/ADR-RES	Breast Cancer	PC.3	Prosinte Concer	SN12C	A498	Renal Cancer 786-0	SK-OV-3	OVCAR-5	Ovarian Carcer IGROVI	UACC-257	SK-MEL-28	SK-MEL 2	LOX IMM	Melanoma	SNB-75	SP-539	SP-295	CNS Cancer	SW-620	HT29	HCT-116	HCC-2998	Colon Cancer COLO 205	NCI-H460 NCI-H522	NCI-H23 NCI-H322M	NCI-H226	EKVX HOP-62	Non-Small Cell Lung Cancer A349/ATCC	RPM1-8226 SR	K-562 MOLT-4	HC0(TB)	Leukemla	Panel/Cell Line
	-5.13	4.66	5.30	.5.63	4.80	.5.21	-5.24 -5.32	:	-4.63 > -4.00	-4.72	> .4.00	3,44	4.77	-4.87	-5.29	-6.08		-5.37		-5.59	-4.56	-5.78	-5.17	-5.31	-5.33 -4.82	4.82	A .00	-5.71	-5.08	-5.01	-5.33 -4.66	4.24 p	-5.06	-5.55 -5.35	-5.17	3.67	-5.57	Log <sub>10</sub> GI50
		_1_	Π	ľ	LL.		-1		L	L			L			T	1			1	1	1			<b>I</b> .,	, I.			-31	<u>, •</u>	1,				<b>[</b>	<u></u>	T	G150
1.27	-4.20	> 4.00	-5.15		-4.19	> -4.00	4.12		> 4.00	> -4.00	× .4.00	-4.28	V 1.00	× 1.00	> -4,00	-4.86	V 1 00 V 1 00	-4.68	v :408	414	> 4.00	454	> .4.00	> 4.00	<u>.</u>	· · · · · · · · · · · · · · · · · · ·	> 4.00	4.99	> -4.00	v v 1.00	> 4.00	> .4.90	v v 1.08	> -4.00	> -4.00 -4.82	> -4.00	4.27	Log <sub>19</sub> TGI
:		1.1	T			-1		1	_1					1.1				1										_	1			<b>.</b> 1			T		Γ	101
.,		V 1. 135	v	> 400	> 1.156	, <b>,</b> , , , , , , , , , , , , , , , , ,	> .4 )0	V 5	0.7.0	·	> .4 S	V .4 92	> .4 00	v v ようさ		/ / k k Š 3	> 14.90	, , ,	v .i. ∂	× <b>k</b> 3	<b>↓</b> ↓ ↓ ↓ ↓	> -4 00	¥ 155		/ <b>.</b>	> .A.150	¥ 1.35	¥	·	v kajo	× 14 150	> .A 5	, , , , , , , , , , , , , , , , , , ,	, 1, 20	44.5	, , , , , , , , , , , , , , , , , , ,	v .4.3	010
-	1					<del>-</del>							-										1		<del></del>			]										-

Experiment ID: 9502RM1c Test Type: 8 Units: Molar

eport Date: March 28, 1995 Test Date: February 13 1 QNS: SHP MC:

OMI: Phomopsinamine A Stain Reagent: Dual-Pass SSPL: 0FLC

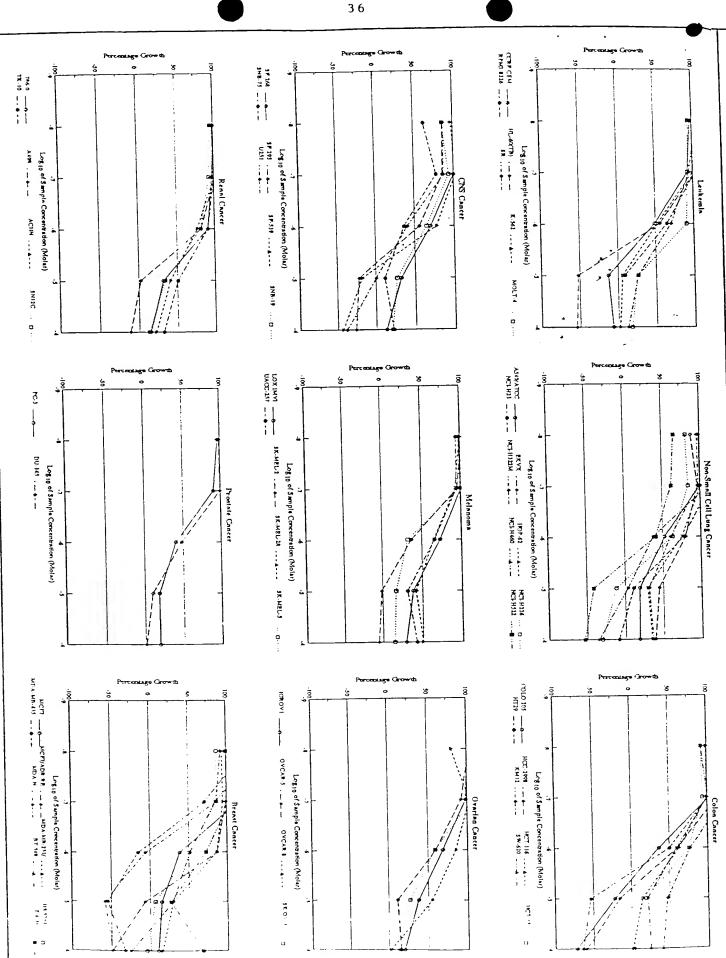
						Locio	Concent	tat.c=					
	Time			Optical		ties			E • : :=:				GISC TGI LCS0
Panel/Cell Line	lero	Ctrl	- £ . C	-7.0 -	-6.0	-5.0	- <b>:</b> . 0	- t C -			1 6 -	•	G. 50 1G. 2C.30
Leukemio	0.634	1 755	1.771	1.754 1	. 367	0.591	0.416	:::	<b>.</b> .	: -		- 2.4	1.€9£-0€
CCRF-CEM HL-60 (TB)		1.622	1.679			0.371	0.312	106	٠.			- 4 7	4.56E-C7 2.60E-06 :1.00E-04
K-562	0.382	1.370		1.366 1		0.369	0.326	100	16:	63	-3 25	-13	1.56E-06
HOLT-4						0.981 0.790	0.793	104	<u>.</u> .	6 E	i	-	1.60E-06 >1.00E-04 >1.00E-04
RPHI-8226						0.412	0.366	10:				-: .	2.64E-07 2.37E-06 1.00E-04
an and Coll lung Canger													
A549/ATCC	0.377	1.339	1.309			0.577	0.447	è.	f .	4.4	E 2		7.06E-07 >1.00E-04 >1.00E-04
EKVX		1.029				0.659	0.629	e ë	11.	- <u>-</u>	41	3 6	5.81E-06 >1.00E-04 >1.00E-04 2.70E-05 >1.00E-04 >1.00E-04
HOP-62	0.391	0.893				0.659	0.970	128	::::	:::	3.5	3 5	>1.00E-04 >1.00E-04 >1.00E-04
HOP-92	0.761	1.116			0.729	0.525	0.446	114	114	4.7	-14	- 17	8.95E-07 5.99E-06 >1.00E+04
NCI-H226 NCI-H23	0.419	1.166			0.966	0.669	0.674	101	č 1	7.3	3.3	3 4	3.65E-06 >1.00E-04 >1.00E-04
NCI-H322H						0.644	0.785	104	171	7 3 3 7	25 12	17	2.90E-06 >1.00E-04 >1.00E-04 6.35E-07 >1.00E-04 >1.00E-04
NCI-H460	0.181					0.316	0.329 0.316	100	101			-24	3.932-06 3.94E-05 >1.00E-04
NCI-H522	0.413	1.073	1.071	1.084	0.691	0.042	0.510	100					
Colon Cancer COLO 205	0.326	1.333	1.317	1.156	0.606	0.246	0.179	3 9	ΕÏ	2 €	-24	- 45	3.91E-07 3.40E-06 >1.00E-04
HCC-2996		1.266		1.284		0.402	0.396	.:	103	+3	-32	-33	7.55E-07 3.73E-06 >1.00E-04
HCT-116	0.161	1.304	1.219			0.343	0.256	93	£ 3"	50	16 22	€	9.E7E-07 >1.00E-04 >1.00E-04 1.76E-06 >1.00E-04 >1.00E-04
HCT-15	0.317	1.667				0.614	0.393	ع ې	161	4.0		4	6.76E-07 >1.00E-04 >1.00E-04
HT29	0.166	1.445	0.620 1.397			0.397	0.301	96	£ :	2 €	٥	ı	3.70E-07 >1.00E-04 >1.00E-04
KM1.2 SW-620	0.156	0.691			0.660	0.453	0.364	97	£ 3	71	40	3.7	4.69E-06 >1.00E-04 >1.00E-04
CNS Cancer								9.6	ę į	ő 4	47	3.0	6.77E-06 >1.00E-04 >1.00E-04
SF-268		1.431	1.410		1.079	0.920	0.755	103	94 61	24	47	20	3.53E-07 >1.00E-04 >1.00E-04
SF-295	0.400	1.038	1.055		0.554	0.213	0.153	102	٠.	\$3	-45	-60	1.06E-06 3.46E-06 2.09E-05
SF-539 SNB-19	0.571	1.385	1.372	1.336	1.063	0.617	0.742	9.6	è 1	€3	3 C	2.2	2.22E-06 >1.00E-04 >1.00E-04
SNE-75	0.361	0.626	0.664		0.470		0.430	116	:	3-6	10	20	6.51E-07 >1.00E-04 >1.00E-04 6.39E-07 >1.00E-04 >1.00E-04
U251	0.199	0.893	0.920	0.615	0.481	0.273	0.279	104	€ 5	÷ 2	11	: 2	6.39E-07 31.00E-04 31.00E-04
Helenoma				0.942	0.765	0.467	0.357		6 5	7.5	37	2.2	4.66E-06 >1.00E-04 >1.00E-04
LOX IMVI MALME-3M		0.962	1.035	0.942	0.780	0.631	0.610	100	7 :	5.5	56	25	1.57E-06 >1.00E-04 >1.00E-04
MALME-3M	0.196	C. 569	0.564	0.552	0.407	0.201		õõ	ě :	5€	1	- 2	1.31E-06 3.46E-05 >1.00E-04
SK-MEL-2	0.746	1.368	1.364		1.161	0.853	0.646	õĉ	ç :	7.0 6.0	17 24	16	2.40Z-06 >1.00E-04 >1.00E-04 1.94Z-06 >1.00E-04 >1.00E-04
SK-MEL-26		1.166	:			0.725	0.853 0.223	• •	€ :	3.6	27	:0	4.00E-07 >1.00E-04 >1.00E-04
SK-MEL-5	0.034		1.005	0.702 1.246	0.406			203	e 1	7.3	64	7.3	>1.00E-04 >1.00E-04 >1.00E-04
UACC-257 UACC-62		1.662	1.621			1.029		97	5.3	\$ 3	35	37	1.43E-06 >1.00E-04 >1.00E-04
Ovarian Cancer	••••									ءِ -		* 6	E.26E-06 >1.00E-04 >1.00E-04
IGR-OV1	0.515		1.633	1.631	1.445	1.071	0.864	25 201	5 1	1.5	47	30 ~€	2.54E-07 1.53E-05 >1.00E-04
OVCAR-3		0.905	0.910	1.189	0.353	0.301		9.9	101	ēĢ	ءِ ۽	4.5	4.29E-05 >1.00E-04 >1.00E-04
OVCAR-4 OVCAR-5	0.467 0.393			0.914	0.641	0.514		ةة	111	50	25	3.5	1.02E-06 >1.00E-04 >1.00E-04
OVCAR-6	0.267			1.211	1.126	0.658			153	52	42	2.2	6.95E-06 >1.00E-04 >1.00E-04 1.06E-06 >1.00E-04 >1.00E-04
SK-OV-3	0.466	1.011	1.012	0.997	0.747	0.470	0.490	700	ķ -	2.1	U	4	1.062-06 >1.062-04 >1.062 -1
Renal Cancer	6 365	0.949	1.006	0.955	0.716	0.396	0.350	108	11.	€ē	26	2.0	2.79E-06 >1.00E-04 >1.00E-04
786-0 <b>A49</b> 6	0.200			1.470	1.283	1.007			117	€1	- 7	-1€	1.45E-06 7.91E-06 >1.00E-04
ACHN	0.406				1.157	0.970	0.603	102		71	5.3	3.6	1.66E-05 >1.00E-04 >1.00E-04 6.95E-06 >1.00E-04 >1.00E-04
CAKI-1	0.466		0.861	0.663	0.630	0.685		6.6		75 56	45 11	4.6 5.0	>1.00E-04 >1.00E-04
RXF-393	0.704				1.195	0.602		6 6 6 6		79	46	30	6.61E-06 >1.00E-04 >1.00E-04
SN12C	0.371	1.335		1.236	1.133	0.833			3.64	111	7.3	7.3	>1.00E-04 >1.00E-04 >1.00E-04
TK-10 UO-31		1.476		1.513	1.452	1.066		1 C 2	7.6-4	57	53	5.3	>1.00E-04 >1.00E-04 >1.00E-04
Prostate Cancer	- *												5.54E-07 >1.00E-04 >1.00E-04
PC-3	0.302	1.164	1.163	1.039	0.627			102		36 35		10	5.60E-07 . >1.00E-04
DO-145	0.339	1.029	1.031	0.964	0.563	0.299	0.344	100				•	
Breast Cancer MCF7	0.42	3. 1.139	1.163	1.160	0.733	0.620	0.490	103				ċ	7.82E-07 >1.00E-04 >1.00E-04
MCF7/ADP-RES		2.037			0.929	0.65	6 0.476	۰		€ 5		21	6.02E-06 >1.00E-04 >1.00E-04 3.45E-06 >1.00E-04 >1.00E-04
MDA-MB-231/A	TCC 0.40	6. 0.926	0.905	0.676	0.606			103		76 70		- 2	>1 005-04 >1 00E-04 >1.00E-04
HS 578T		4 1.396			1.239			102	. €i			- 27	1.65E-07 1.59E-06 >1.00E-04
MDA-MB-435 MDA-N	0.32			0.910	0.421			. و	4 11	-56			1 G3E-07 2.95E-07 E.46E-U/
BT-549	0.47						2 0.617	11	يب ه	5.2		43	1.43E-06 >1.00E-04 >1.00E-04
T-47D	0.71							ò	3 10:	77	54	¯ <b>€</b>	>1.00E-04 >1.00E-04 >1.00E-04



#### National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results

Z: L _73165 -K / 0-1 / 5	Experiment ID: 9409SC89	Test Type: 8	Units: Molar
ort Date: October 27, 1994	Test Date: September 26, 1994	QNS:	MC:
MI: PHOMOPSINAMINE A	Stain Reagent: Dual-Pass	SSPL: 0FLC	

						Log10	Concent	ration							
	Time		Meas	n Optica	al Densi	ties				ent Gr					
inel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-6.0	-7.0 -	-6.0 -	5.0	-4.0	GI50	TGI	TC 20
eukemi a				. 252	0.516	0.216	0.232	97	93	49	-13	-7	9.50E-07	6.21E-06	>1.00F-04
CCRF-CEM	0.250	0.793	0.779 0.710	0.757 0.706	0.516	0.101	0.096	104	3 6 3	56	-53	-55	1.13E-06		9.47E-06
HL-60(TB)	0.213	0.691	0.710	0.764	0.463	0.165	0.141	105	100	53	6	2		>1.00E-04	
K-562	0.129	0.762	1.312	1.293	1.266	0.563	0.469	95	23	91	26	17			>1.00E-04
HOLT-4	0.281	1.366	0.919	0.899	0.640	0.255	0.258	106	103	65	9		1.86E-06		
RPMI-8226	0.196	1.679		1.612	1.256	0.614	0.414	104	95	71	2€	12		>1.00E-04	>1.00F-04
SR	0.238		1./41	1.012	1.230	0.014	0.41.	•			-				
on-Small Cell Lun	0 361	1.610	1.591	1.608	1.016	0.596	0.584	66	200	53	19	16	1.19E-06	>1.00E-04	>1.00F-04
AS49/ATCC	0.688	1.691	1.579	1.652	1.493	1.128	1.074	69	96	0.3	44	3.8	6.79E-06	>1.00E-04	>1.00E-04
EKVX	0.834	1.662	1.701	1.666	1.457	1.074	1.115	105	201	75	29	34	3.51E-06	>1.00E-04	>1.00E-04
HOP-62	0.591	1.104	1.010	1.024	0.913	0.521	0.409	82	64	63	-12	-31	1.48E-06	6.95E-06	>1.00E-04
NCI-H226 NCI-H23	0.455	1.521	1.625	1.647	1.288	0.571	0.413	110	112	78	11	-9	2.62E-06	3.48E-05	>1.00E-04
NCI-H322M	0.556			1.454	1.114	0.842	0.867	96	97	61	31	36			>1.00E-04
NCI -H460	0.219		1.184	1.252	0.563	0.252	0.142	104	111	37	4	-35	€.72E-07		>1.00E-04
NCI-H522	0.434	1.347		1.000	0.803	0.254	0.201	66	€2	40	-42	-54	3.58E-07	3.11E-06	4.86E-05
olon Cancer															
©LO 205	0.208	1.003	1.074	1.023	0.495	0.163	0.059	109	203	36	-22	-72			3.65E-05
HCC-2998	0.262	0.891	0.947	0.974	0.642	0.221	0.107	109	713	60	-16	-59			6.16E-05
HCT-116	0.230	1.465	1.453	1.458	1.003	0.406	0.237	99	ō ö	63	14	1			>1.00E-04
ACT-15	0.717	2.858	2.699	2.730	2.337	1.121	0.760	93	94	76	19	2			>1.00E-04
RT29	0.148	0.793	0.801	0.803	0.470	0.069	0.054	101	102	50	-53	-64			9.27E-06
RM1.2	0.907	2.189	2.312	2.489	1.895	1.506	1.4.8	110	123	77	47	40			>1.00E-04
SW-620	0.140	0.828	0.778	0.831	0.549	0.283	0.306	93	100	59	21	24	1.75E-06	>1.00E-04	>1.00E-04
NS Cancer													2 225 26		
SF-268	0.367	1.284	1.294	1.284	1.008	0.659	0.484	101	100	70	32	13			>1.00E-04
SF-295	0.554	1.381	1.270	1.263	1.016	0.431	0.405	67	86	56	-22	-27			>1.00E-04
SF-539	0.517	1.568	1.540	1.592	1.331	0.423	0.291	97	102	77	-18	-44			>1.00E-04 >1.00E-04
SNB-19	0.587			1.571	1.265	0.866	0.800	86	94	65 36	27	20 22			>1.00E-04
SNB-75	0.367		0.701	0.763	0.560	0.428	0.483	63	7 E 6 7	40	11	-39			>1.00E-04
<del>0</del> 251	0.191	0.834	0.753	0.753	0.451	0.193	0.117	€ 7	6 /	40	U	-39	6.23E-07	1.026-02	71.00L-04
sel anoma							0 503	3.0	101	73	38	26	4 SSE-06	>1 00E=04	>1.00E-04
TOX IMAI	0.279		1.050	1.071	0.852	0.576	0.503	102	96	37	-1	-6			>1.00E-04
SK-MEL-2	0.563		1.516	1.462	0.905	0.555	0.530	102	93	65	42	49			>1.00E-04
SK-MEL-28	0.305		0.974	0.929	0.740	0.584	0.542	102	99	32	17	14			>1.00E-04
SK-MEL-5	0.354		1.704	1.671	0.778 1.564	1.111	1.252	95	9.5	66	31	42			>1.00E-04
<b>DACC-257</b>	0.709	2.006	1.941	1.943	1.564	1.111	1.232	,,,		00		••	2.000		
Warian Cancer		. 470	1.482	1.460	1.125	0.769	0.565	100	9.6	69	37	19	3.96E-06	>1.00E-04	>1.00E-04
IGROVI	0.346			0.834	c.671	0.432	0.451	102	93	60	11	15	1.58E-06	>1.00E-04	4 >1.00E-04
OVCAR-5	0.550		1.238	1.426		1.016		61	103	85	55	2	1.22E-05	>1.00E-04	4 >1.00E-04
OVCAR-8 SK-OV-3	0.330				0.705	0.551		101	107	59	27	14	1.88E-06	>1.00E-04	4 >1.00E-04
	0.423	0.901	0.500	0											
Renal Cancer 786-0	0.434	2.015	2.010	1.977	1.875	0.929	.0.664	100	98	91	31	15			4 >1.00E-04
786-0 A498	0.561				0.906	0.570		111	101	82	2	-11			5 >1.00E-04
ACHN	0.306				1.041	0.692	0.508	6 ق	100	77	41	21	5.50E-06	>1.00E-0	4 >1.00E-04
SN12C	0.636				1.483	0.981	0.770	9€	93	82	33	13	4.52E-0	>1.00E-0	4 >1.00E-04
1K-10	0.399			0.998	0.944	0.700	0.585	9.6	100	91	50	31	1.05E-05	>1.00E-0	4 >1.00E-04
Prostate Cancer															
PC-3	0.952	3.445	3.372	3.208	1.952	1.405	1.413	<u>9</u> 7	90	40	18	16			4 >1.00E-04
100-145	0.459	1.595	1.581	1.567	0.999	0.572	0.467	55	99	4 6	10	1	8.97E-0	/ >1.00E-0	4 >1.00E-04
Breast Cancer													3 005 0		4 N 00E-04
HCF7	0.259	1.158	1.285			0.390		114	116	38	15	10			4 >1.00E-04
MCF7/ADR-RES	0.517	1.304				0.481		103	99	67	-7	-48			6 >1.00E-04 4 >1.00E-04
MDA-MB-231/ATC	C 0.614	1.602		. 1.559		0.902		95	96	86	29	15			5 >1.00E-04
HS 578T	0.586	1.164		1.067		0.623		87	£7	50	. 6	-5	1.02E-0		
MDA-MB-435	0.283					0.128				-15			1.75E-0 2.49E-0		
MDA-N	0.332		. 14348			0.139				-€			1.14E-0		5 >1.00E-04
BT-549	0.606										29			3.4/E-0	4 >1.00E-04
T-47D	0.775	5 1.915	1.907	1.973	1.601	1.072	1.547	ءَ ہَ	205	72	26	68	•	71.00E-0	1.00L 04



MQ_MID Delia Range	MDA:MB-433 MDA:N BT-549 T-47D	MDA-MB-231/ATCC HS 578T	Breat Cancer MCF7 MCF7 ACTIVADE DES	Prostate Cancer PC-3 DU-145	SN12C TK-10	786-0 A 498	OVCAR-8 SK-OV-3	IGROVI OVCAR-S	SK-MEL'S	SK-MEL-28	Melanoma LOX IMVI	SNB-75 U251	SF-539 SF-539	CNS Cancer SP-268	KM12 SW-620	HCT-15 HT29	HCC-2998 HCT-116	Colon Carcer COLO 205	NCI-H450 NCI-H522	NCI-H23	HOP-62 NCI-H226	AS49/ATCC	RPMI-8226 SR SR Cell Lung Cancer	K-562 MOLTA	出しるの(工事)	Leukemia COR T CEM	Panel/Cell Line
-5.76 1.00 1.84	5.94	5.36 5.76	4.15 -5.60	4.20 4.05	4.98	-5.31 -5.60	4.91 -5.73	-5.40 -5.80	3.55	5.36 6.27	.534	6.33 6.20	5.71 5.61	-5.48 -5.07	-5.76	5.55 5.00	-5.86 -5.74	6.21	5.17 5.45	-5.58 -5.64	-5.45 -5.83	-5.92 -5.17	333	-5.37 -5.37	5.95	-6.02	Log <sub>In</sub> GE0
		Ţ,¹	- I	П	l	LJ		L		1	1	I	<b>R</b> =	.1			■,	-1	1		ل	J,	1	_1	··	<b>T</b>	GI50
218	5.06 5.46 > 4.00	5.1.4.80	> 4.00 -5.07	× × × × × × × × × × × × × × × × × × ×	× 4.00	S 22 83 4 4 4 4	> 4,00	V V V	> 4,00	V 4.00	> 4.00 5.04	4.99	> 4.00	> 4.00 -5.29	> 4.00	3.52 > 4.00	V 100 000 1	.5.38 -5.21	3.51	V 1.00	5.16	, , , , , , , , , , , , , , , , , , , ,	> 4.00	> 4.00	> 4.00	3.21	Log <sub>10</sub> TGI
0										<u></u>	T	T				1	<u>[]</u>	Π		Γ'						Π	161
108	88 7 7 8 8 7 7 8 8 9 7 8 9 8 9 9 9 9 9 9	× × × × × × × × × × × × × × × × × × ×	888	\$ \$ \$ \$ \$	5 4 8 8 4 8	. 44 . 28 . 33 . 33 . 33 . 33 . 33 . 33 . 33 . 3	7	388	2	· · · · · · · · · · · · · · · · · · ·	2	× ±3	333 333	V V V 4 4 4 2 5 5	× 400	> 4.33 4.33	∨ ∨ 4 4 ≿ ≿	F F	4.2	v v З З	 24.4 25.5 25.5 26.5 26.5 26.5 26.5 26.5 26.5	 4 4 5 5	5		 8 4 8 3	400 302	2810
0									3	• •		-														T	

#### Example 2

The following data show the effect of phomopsin A on several human cancer cell lines growing *in vivo* in hollow fibres inserted subcutaneously and intraperitoneally in athymic mice, as employed by NCI to assess the *in vivo* anticancer potential of compounds (Hollingshead *et al.*, 1995). Significant cell growth inhibition and cytocidal activity in demonstrated.

Report printed on 07-MAY-97

SEX: F	14. TE	ELABOATI N DATE: 15-REC-95 S RACK/INNE: 1		HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	Nudes		IMPLAN STAGIN	IMPLANT DATE: CB-DEC-95 STAGING DATE: 11-DEC-95	C8-DEC-9
					,		%T/C	D		
		TREATMENT			LOX IMVI	IMVI	OTOD	colo 205	OVCAP-3	19-3
Grp NSC No. No.	Sose/Units	કા. જેવા કર્યા છ	No. of No. of Mice Fibers	No. of Fibers	1.0	SC	IP	SC	ŢP	SC
5' D-673162	30.00 mg/kg/dose	30.00 mg/kg/dosm IP QD · 4, Da, 3	ю	3	>100	>100	63	6.0	35	ол 1-
58 0-673162	20,00 mg/kg/dose	20.00 mg/kg/dose IP QD + 4, Sa, 3	٤	٣	, 37	>100	5.8	8.5	36	>100

	-Besog)
	6731627
	NSC .
VEHICLES	Grp 57 -> Grp 58 ->

Inj. Vol.:0.1 ml/10gm body wt Inj. Vol.:0.1 ml/10gm body wt	
(Unknown) (Unknown)	
.01) in Saline + Tween 80 (0.05%) (Unknown)	
Line + Twee	
es ut	
Dose-	
673162. 6731627	
NSC .	
^ ^	

#### COMMENTS for HF591-0-HF

Report printed on 07-MAY-97

EXPT NO: HF590-0-HF SEX: F	3H-	EVALUATION DATE: 15-DEC-95 source/DINE: 1	HOST: Athyr SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	ndes		IMPLAN	IMPLANT DATE: 07-DEG-95 STAGING DATE: 11-DEC-95	07-DEG-9 11-DEC-9
	TR	TREATMENT		,	23	%T/C	1-231	- <b>M</b> .5	SW-620
	Oseo/IIntre	Rr Schedule	No. of No. of Mice Fibers	IP	SC	IP	SC	11.	SC
57 D-673162	30.00 mg/kg/dose	30.00 mg/kg/dose IP QD X 4, Day 4	3	81	96	. 46	72	>100	>160
58 D-673162	20.00 mg/kg/dose	20.00 mg/kg/dose IP QD X 4, Day 4	3	>100	>100	44	46	>100	>100

HICLES  NSC # 673162/ 1 (Dose= 30.00) : In Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt	
(Unknown) (Unknown)	
0 (0.05%) 0 (0.05%)	
+ Tween 8 + Tween 8	
in Saline in Saline	
30.00) :	
1 (Dose	38001
673162/	1701010
NSC	NSC -
VEHICLES  Grp 57 -> NSC 1	Grp 38 -> NSC

COMMENTS for HF590-0-HF

Report printed on 01-APR-96

EXPT NO: HF590-0-HF SEX: F		EVALUATION DA SOTRCEZLINE	EVALUATI N DATE: 15-DEC-95		HOST: Athyn SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	Nudes		IMPLA	IMPLANT DATE: 07-DEC-95 STAGING DATE: 11-DEC-95	07-DEC-9 11-DEC-9
								%T/C (Net Growth)	Growth)		
		TREATMENT			,	NCI-H23	.н23	MDA-MB-231	B-231	MS	SW-620
Orp NO.	Dose/Units	Rt	Schedule	Mo. of	Mice Fibers	IP	SC	IP	SC	IP	SC
5 1 D-673162	30.00 mg/kg/dose IP QD = 4, Day 4	IP QD 4, C	Jay 4	Е	e	16	94	30	63	>100	>100
58 D-673162	20.00 mg/kg/dosa IP QC 4, Da, 4	IP QC 4, C	,a, 4	3	Э	>100	>100	28	29	>100	>100

#### VEHICLES

673162/ 1 (Dose- 10.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 1 (Dose- 10.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt NSC # 3rp 57 -> 3rp 58 ->

#### COMMENTS for HF590-0-HF

## Report printed on 01-APR-96

EXPT NO; HF591-0-HF SEX: F	EVALUATION DATE: 15-DEC-95 SOURCE/LINE: 1	HOST. SOURC	HOST: Athymic Nudes SOURCE: APA	I.S.	IMPLANT DATE: 08-DEC-95 STAGING DATE: 11-DEC-95	-DEC-95
				%I/C (Net Growth)		
	TREATMENT		LOX IMVI	CO1.O 205	OVCAR-3	
Grp NSC No. No.	Dose/Units Rt Schedule	No. of No. of Mice Fibers	IP SC	IP SC	dI	SC
57 D-673162	30.00 mg/kg/dose IP QD X 4, Day 3	3 3	>100 >100	59 34	- 18	22
58 D-673162	20.00 mg/kg/dose IP QD X 4, Day 3	3 3	29 >100	48 81	-15	>100

## COMMENTS for HF591-0-HF

NSC #

Grp 57 -> Grp 58 ->

VEHICLES

673162/ 1 (Dose- 30.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 1 (Dose- 20.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt

Report printed on 07-MAY-97

EXPT NO: HF581-0-HF SEX: F	H.	EVALUATION S CONTROL S	EVA CATION DATE: 17-NOV-95 \$ 100 P P P P P P P P P P P P P P P P P P		HOST: Athyr SOURCE: AFA	HOST: Athymic Nudes SOURCE: APA	S		STAGII	STAGING DATE: 13-NOV-95	13-NOV-
	α. 	TREATMENT	•			NCI - 1952		%T/C	-62	:	1252
Grp NSC No. No.	Dose/Units	Rt	Schedule	No. of No. of Mise Fibers	No. of Fibers	IP	SC	IP	SC	IP	SC
0-673162	30,000 mg/km, mase (IP) Jihoo G. Gaood	IF 30 - 1. 24.	17	мм	r. m	85	96	100	92	>100	86
8 0-673162	20.30 mg/kg dose IP 3D + 4, Da, 4	IP 3D · 1, Da,	y	m m	3 2	07	>100	76	06	06	66

#### (Dose- ...)) in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt : (Dose- ...)) in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162: 673162: NSC . Crp 7 -> VEHICLES

COMMENTS for HF581-0-HF

## Report printed on 01-APR-96

EXPT NO: HF581-0-HF SEX: F	(L.	EVALUATION DATE: 17-NOV-95 SOURCE/LINE: 1		HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	indes		IMPLAN	IMPLANT DATE: STAGING DATE: 13-NOV-95	3-VON-E1
	Ē	, , , , , , , , , , , , , , , , , , ,					%I/C (Net Growth)	Growth)	i	
		נבט וווביא ז		,	NCI-H522	15.22	UACC-62	-62	U251	51
Grp NSC No. No.	Dose/Units	Rt Schedule	Mice Fibers	Fibers	IP	SC	IP	SC	16	SC
) D-673162	30.00 mg/kg/dose	30.00 mg/kg/dose IP QD X 4, Day 4	мм	3 2	59	91	100	80	>100	9.1
8 D-673162	20.00 mg/kg/dose	20.00 mg/kg/dose IP QD X 4, Day 4	m m	3 2	18	>100	95	67	83	86

#### VEHICLES

Inj. Vol.:0.1 ml/10gm body wt	Inj. Vol.:0.1 ml/10gm body wt
(Unknown)	(Unknown)
Tween 80 (0.05%)	Tween 80 (0.05%) (Uni
: in Saline + 1	: in Saline + 1
30.00) :	20.00)
1 (Dose-	1 (Dose-
673162/	673162/
NSC #	NSC #
Grp 7 ->	Grp 8 ->

### COMMENTS for HF581-0-HF

Report printed on 07-MAY-97

SXFT NO: HF582-0-HF SEX: F		CALATION DATE: 17-NOV-95 CORCECTINE	HOST SOURCE	HOST: Athymic Nudes SOURCE: APA	s		STAGIL	IMPLANT DATE: 33-NO7-95	33-NOV-93
	TREA "MENI.			, , , , , , , , , , , , , , , , , , ,	35	%T/C OVCAR-5	-5	Sie	SF-295
Grp NSC	Dose/Units Rt	Schedule	No. of No. of Mice Fibers	IP	SC	ПР	SC	IP	SC
. 2-673162	30,00 mg/k1/dose (P. QD Y 4, Durk 4	20 × 4. Day 4	3 2	17.	69	(8)	7.6	on ex	0 0 10
3 0-673162	20,00 mg/kg/dose IP QD 14, D4, 4	20 + 4, 20, 4	9	81	8.7	68	9.5	>100	2014

# 673152/ 1 (Dcse- 1).00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. 701.:0.1 ml/10gm body wt 673152/ 1 (Dcse- 1).00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. 701.:0.1 ml/10gm body wt Grp 7 -> NSC # Grp 8 -> NSC #

VEHICLES

COMMENTS for HF582-0-HF

## Report printed on 01-APR-96

EXPT NO: HF582-0-HF SEX: F	0-HF	EVALUATION DATE: 17-NOV-95 SOURCE/LINE: 1	NOS	HOST: Athymic Nudes SOURCE: APA		IMPLANT DATE: STAGING DATE: 13-NOV-95	13-NOV-95
3					%I/C (Net Growth)	th)	
	TRE	TREATMENT	1	MDA-MB-435	OVCAR-5	SF	SF-295
Grp NSC No. No.	Dose/Units R	Rt Schedule	No. of No. of Mice Fibers	I IP SC	IPS	SC IP	SC
7 D-673162.	30.00 mg/kg/dose IP QD X 4, Day 4	P QD X 4, Day 4	3 2 3 3	62 58	38	89 06	>100
8 0-673162	20.00 mg/kg/dose IP QD X 4, Day 4	.P QD X 4, Day 4	3 3	74 82	87 9	94 >100	>100

#### VEHICLES

inj. Vol.:U.i mi/i∪gm body wt Inj. Vol.:O.i ml/lOgm body wt	
(Unknown) (Unknown)	
673162/ 1 (Dose- 30.00) : In Saline + Tween 80 (0.051) (Unknown) 673162/ 1 (Dose- 20.00) : In Saline + Tween 80 (0.051) (Unknown)	
1 (Dose	
673162/ 673162/	
> NSC +	
Grp 7 -> NSC   Grp 8 -> NSC	

### COMMITS for HIS82-0-HF

## Report printed on 01-APR-96

EXPT NO: HF580-0-HF SEX: F	Ĺ.	EVALUATION DATE: 09-NOV-95		HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	Vudes		IMPLAN STAGIN	IMPLANT DATE: STAGING DATE: 05-NOV-95	05-NOV-95
	C NGME A G G G	·· NAM					%I/C (Net Growth)	Growth)		
	T COURT		;   	, 1	LOX IMVI	IMVI	COLO	COLO 205	0AC	OVCAR-3
No. No.	Dose/Units Rt	Schedule	Mice Fibers	Fibers	IP	SC	IP	SC	IP	SC
D-673162	45.00 mg/kg/dose IP QC × 4, Esy 2	QC x 4, Fay 2	e	1	86	0.8	>100	64	61	>100
8 D-673162	30.00 mg/kg/dose IP QE × 4, Day 2	QC × 4, Day 2	3	е	88	8.5	58	986	25	37

#### VEHICLES

Inj. Vol.:0.1 ml/10gm body wt	1 ml/10gm body wt
Vol.:0.1	nj. Vol.:0.1
Inj.	Inj.
J.05%) (Unknown)	(Unknown)
(0.05%)	(0.05%)
Tween 80	sen 80
: in Saline +	: in Saline + Twe
45.00)	10.00
-esod) 1	-esod)
673162/	673162/
NSC #	NSC •
۲ - ۲	^ &
Grp	Grp 8 ->

#### COMMENTS for HF580-0-HF

## Report printed on 01-APR-96

EXPT SEX.	EXPT NO: HFS79-0-HF SEX: F	EVALUATION DATE: 09-NOV-95 SOURCE/LINE: 1		HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	Nudes		IMPLAN STAGIN	IMPLANT DATE: 02-NOV-95 STAGING DATE: 05-NOV-95	02-NOV-95 05-NOV-95
							%T/C (Net Growth)	Growth)		
		TREATMENT	I		NCI-H23	423	MDA-	MDA-MB-231	SW-620	620
Grp No.	Grp NSC Dose/Units	Rt Schedule	No. of No. of Mice Fibers	No. of Fibers	11	SC	IP	SC	IP	SC
_	62	45.00 mg/kg/dose IP QD X 4, Day 3	e .	2	4 4	-41	>100	>100	78	78
<b>c</b>	8 D-673162 30.00 mg/kg/dos	30.00 mg/kg/dose IP QD X 4, Day 3	3	3	09	21	66	>100	97	9.8

#### VEHICLES

[n]. Vol.:0.1 ml/10gm body wt	nj. voi.:u.i mi/logm body #c
(Unknown)	(nwouxun)
0 (0.05%)	(0.05%)
+ Tween 8	+ Tween 8
Saline	: in Saline
se= 45.00) : in	30.00)
1 (Dose=	1 (Dose-
673162/	673162/
NSC	NSC .
Grp 7 ->	^ &
Grp	Grp

## COMMENTS for HF579-0-HF

Report printed on 07-MAY-97

EXPT NO: HF580-0-HF SEX: F	4.	ALC CRS	TABLUATION DATE: 09-NOV-95		HOST: Athy SOURCE: APA	HOSI: Athymic Nudes SOURCE: APA	udes		IMPLAN	IMPLANT DATE: 05-NCV-95	05-NCV-9
								),T#	. ن ر		
	TA	TREATMEN		1		LOX IMVI	IMAI	0700	COLO 205	OVCAR-3	R-3
Grp NSC	Dose/Units	Rt	Schedule	No. of Mice	No. of No. cf Mice Fibers	IP	SC	IP	SC	IP	S
. 2-673162	45.00 mg/kg/dose II QI * 4, Lay 2	11 01 14.	. Lay 2	3	1	86	84	>100	72	97	>100
8 D-673162	30.00 mg/kg/dose IF QL > 4, bay 2	IF 01 > 4,	. Day 2	ĸ	м	06	88	67	83	9	93

#### VEHICLES

1 (Dose- '5.30) : In Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt ( Orse- 0.30) : In Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 673162/ NSC + Grp 7 -> Grp 8 ->

#### COMMENTS for HF580-0-HF

Report printed on 07-MAY-97

Grp         NSC         No. of No. of No. of Mice         No. of No. of Mice         Ilbers           No.         No. of No. of Mice         Ilbers         IP           No. of No. o	HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	IMPLANSTAGIN	IMPLANT DATE: 02-NOV-95 STAGING DATE: 05-NOV-95
TREATMENT  No. of No. of  Dose/Units Rt Schedule Mice Fibers IF  62 45.00 mg/kg/dose IP QD X 4, Day 3			\$1/C	
Dose/Units Rt Schedule 62 45.00 mg/kg/dose IP QD X 4, Day 3	1	NCI-H23	MDA-MB-231	SW-620
62 45.00 mg/kg/dose IP QD X 4, Day 3	No. of No. of Mice Fibers	IP SC	IP SC	IP SC
	3 2	(88 (88	>100 >100	8 2 8.
8 D-573162 30.00 mg/kg/dose IP QD X 4, Day 3	3	77 65	99 >100	68 86

# VEHICLES

673162/ 1 (Dose- 45.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 1 (Dose- 30.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt NSC # Grp 7 -> Grp 8 ->

COMMENTS for HF579-0-HF

Finally, it is to be understood that various alterations, modifications and/or additions may be introduced into the composition and/or arrangement of steps previously described without departing from the spirit or ambit of the invention.

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DATED: 29 September, 1999

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**COMMONWEALTH SCIENTIFIC &** 

10 INDUSTRIAL RESEARCH ORGANISATION

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